LIVER FUNCTION TESTS

IN

CONGESTIVE CARDIAC FAILURE

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BONAFIDE CERTIFICATE

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CONTENTS

LIST OF ABBREVATIONS

1. LFT Liver function tests
2. AST/ SGOT Aspartate aminotransferase -serum glutamic oxaloacetic transaminase
3. ALT/SGPT Alanine aminotransferase-serum glutamic pyruvate transaminase
4. CPC chronic passive congestion
5. CLN centrilobular necrosis
6. CHC central hemorrhagic necrosis
7. RHD Rheumatic heart disease
8. CAHD Coronary atherosclerotic heart disease
9. HHD Hypertensive heart disease

AIMS OF THE STUDY

1. To study the liver function tests in congestive cardiac failure.

2. To observe any differences in liver function tests with the etiology of congestive cardiac failure.

3. To study the relationship between liver function test and remission and exacerbation of congestive cardiac failure.

4. To study whether liver function tests can be used as a prognostic indicator in cases of congestive cardiac failure.

INTRODUCTION

The liver has been called the custodian of milieu interior [5]. So any liver disorders will have far reaching consequences on body's homeostasis. Also, numerous pathologies of other systems can affect liver.

Both acute and chronic heart failure may result in abnormalities of liver. Liver receives 25% of cardiac output, that a fall in cardiac output will result in hepatic hypoperfusion. Liver has the capacity to withstand changes in blood flow by vasoactive mechanisms and oxygen extraction from blood. However when critical levels are reached, hepatic injury ensues[16].

Both Right and left sided heart failure can result in liver injury. In right -sided heart failure, elevation of right heart pressure resulting in raised pressure in hepatic sinusoids, hepatic congestion and liver cell hypoxia. In left sided heart failure, decreased cardiac output results in hepatic hypo perfusion and hypoxia. The common pathway is centrilobular hepatocellular necrosis. Zone 3 of the liver lobule is most vulnerable to hypoxic injury due organization of hepatic blood flow.

In this study, the effects of congestive cardiac failure on liver and its function is analyzed in 75 patients compared with 20 healthy individuals. Various etiologies of congestive cardiac failure have been included and

compared, based on their effects on liver functions. Remissions and exacerbations have been tracked on the 7th day and the variations of liver function have been recorded and an attempt has been made to find whether liver function tests can be used as prognostic indicators of congestive cardiac failure.

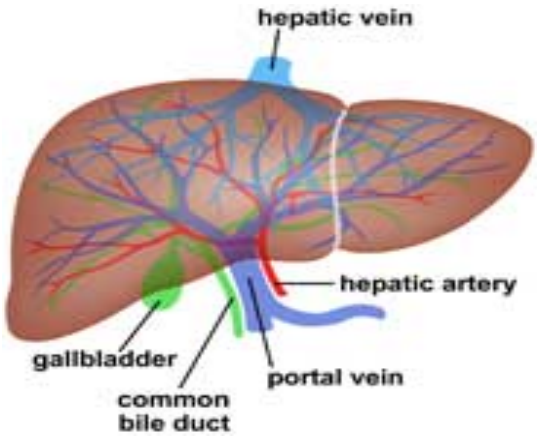
Understanding anatomy and functions of liver, liver enzymes, causes and various forms of congestive cardiac failure and their manifestations, pathology of liver in heart failure are needed before evaluating abnormalities of liver function tests in congestive heart failure.

REVIEW OF LITERATURE

ANATOMY AND FUNTIONS OF LIVER

Liver is the largest organ of the body weighing around 1.5kg. The size and shape of the liver vary and generally match the general body shape—long and lean or squat and square. The liver is located in the right upper quadrant of the abdomen under the right lower rib cage against the diaphragm and projects for a variable extent into the left upper quadrant. The liver is held in place by ligamentous attachments to the diaphragm, peritoneum, great vessels, and upper gastrointestinal organs.

The liver has dual blood supply. The portal vein brings blood from the gut and hepatic artery supplies arterial blood. Hepatic vein drains the liver into inferior vena cava. Porta hepatis is fissure through which vessels enter liver where, Portal vein and hepatic artery divides into branches to right and left lobes. Similarly right and left hepatic ducts join here to form common hepatic duct. Hepatic nerve plexus derives its supply from sympathetic chain T7-T11, left and right vagus nerve and right phrenic nerve. Lymphatic drainage is into small group of glands near porta hepatis. Liver receives 1500ml of blood per minute, mainly through portal vein and 25% through hepatic artery.

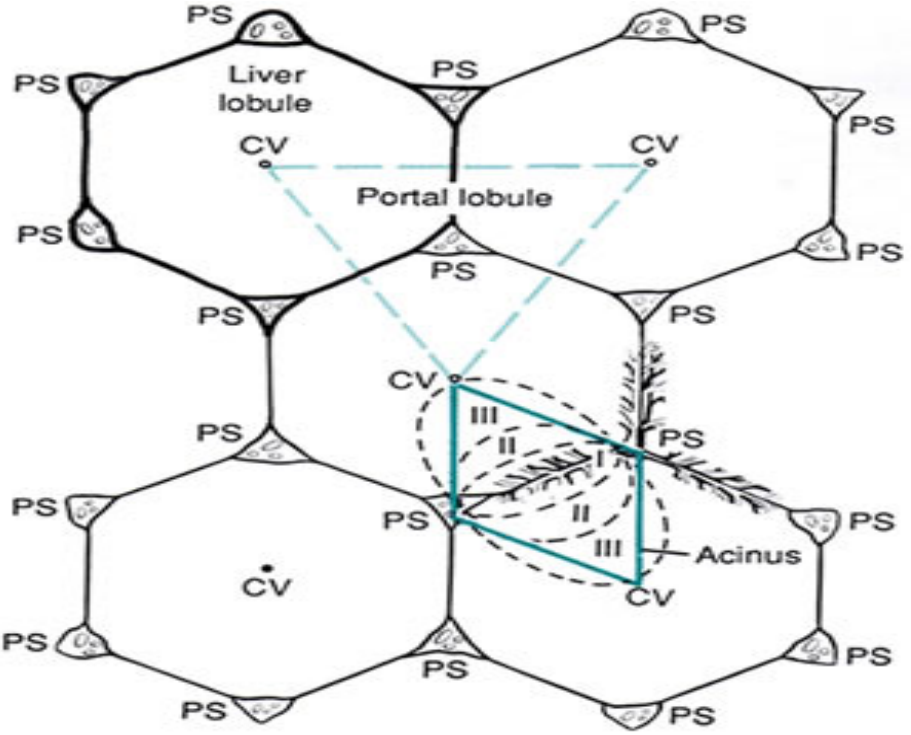


FUNCTIONAL ANATOMY:

The majority of cells in the liver are hepatocytes, which constitute two-thirds of the mass of the liver. The remaining cell types are Kupffer cells (reticuloendothelial cells), stellate (Ito or fat-storing) cells, endothelial cells and blood vessels, bile ductular cells, and supporting structures. In light microscopy, the liver appears to be organized in lobules, with portal areas at the periphery and central veins in the center of each lobule.

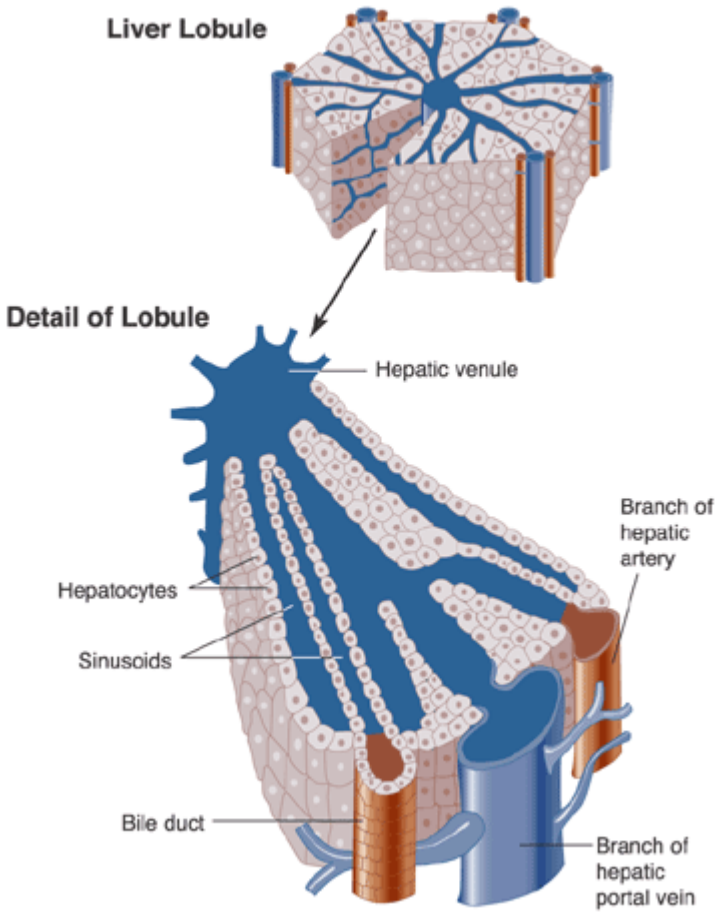
However, from a functional point of view, the liver is organized into **acini**, with both hepatic arterial and portal venous blood entering the acinus from the portal areas (zone 1) and then flowing through the sinusoids to the terminal hepatic veins (zone 3); the intervening hepatocytes constitute zone 2.

The *advantage of viewing the acinus as the physiologic unit of the liver is that it helps to explain the morphologic patterns and zonality of many vascular and biliary diseases not explained by the lobular arrangement.*



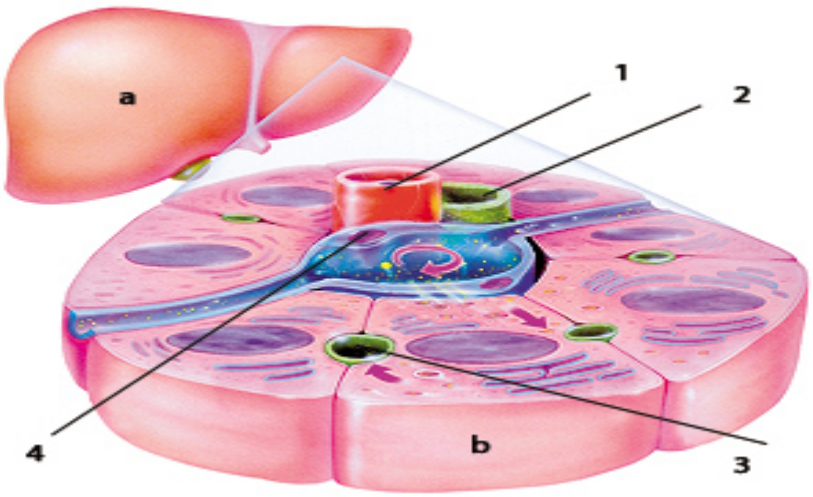
Portal areas of the liver consist of small veins, arteries, bile ducts, and lymphatics organized in a loose stroma of supporting matrix and small amounts of collagen. Blood flowing into the portal areas is distributed through the sinusoids, passing from zone 1 to zone 3 of the acinus and draining into the terminal hepatic veins ("central veins"). *Hence zone 3 of the liver is vulnerable to hypoxic injury*. Secreted bile flows in the opposite direction, in a countercurrent pattern from zone 3 to zone 1. The sinusoids are lined by unique endothelial cells that have prominent fenestrae of variable size, allowing the free flow of plasma

but not cellular elements. The plasma is thus in direct contact with hepatocytes in the space of Disse.



Hepatocytes have distinct polarity. The basolateral side of the hepatocyte lines the space of Disse and is richly lined with microvilli; it demonstrates endocytotic and pinocytotic activity, with passive and active uptake of nutrients, proteins, and other molecules. The apical pole of the hepatocyte forms the cannicular membranes through which bile components are secreted. The canniculi of hepatocytes form a fine network, which fuses into the bile ductular elements near the portal areas.

Kupffer cells usually lie within the sinusoidal vascular space and represent the largest group of fixed macrophages in the body. The stellate cells are located in the space of Disse but are not usually prominent unless activated, when they produce collagen and matrix. White blood cells can migrate through or around endothelial cells into the space of Disse and from there to portal areas, where they can return to the circulation through lymphatics.



1. hepatic artery 2.bile duct 4. portal vein.

The relative functions of cells in the periphery of acini, zone 3 are different from those of cells in zone 1(periportal). Kreb's cycle enzymes are found highest in Zone 1. Glutamic synthetase is found in perivenous cells. Zone3 is vulnerable to hypoxic insult. *Congestive cardiac failure affects zone 3* of the liver resulting in characteristic features.

FUNCTIONS OF THE LIVER:

Hepatocytes perform numerous and vital roles in maintaining homeostasis and health.

Synthetic functions:

These functions include the synthesis of most essential serum proteins (albumin, carrier proteins, coagulation factors 2,7,9 and 10 , many hormonal and growth factors), the production of bile and its carriers (bile acids, cholesterol, lecithin, phospholipids).

Metabolism:

The regulation of nutrients (glucose, glycogen, lipids, cholesterol, amino acids) such as uptake of glucose after a meal, aminoacids used for synthetic functions, production of very low density lipoproteins, metabolism of high and low density lipoproteins and conjugation of lipophilic compounds

Excretory functions:

Liver metabolises bilirubin, bile salts, many drugs and alcohol

Storage functions:

Storage of vitamins B12, A,D, Iron and Copper.

Reticulo-endothelial function:

Liver acts as a microbe barrier for the portal venous blood from the gut through kupffer and other cells. It also detoxifies toxins

Heat production:

Liver carries out various anabolic and catabolic reactions. One of by- products of these reactions is heat, helping in thermostasis.

LIVER FUNCTION TESTS:

Measurement of these activities to assess liver function is complicated by the multiplicity and variability of these functions. The most commonly used **liver "function" tests** are measurements of serum bilirubin, albumin, and prothrombin time.

The serum bilirubin level is a measure of hepatic conjugation and excretion, and the serum albumin level and prothrombin time are measures of protein synthesis. Abnormalities of bilirubin, albumin, and prothrombin time are typical of hepatic dysfunction. Frank liver failure is incompatible with life, and the functions of the liver are too complex and diverse to be sub served by a mechanical pump; dialysis membrane; or concoction of infused hormones, proteins, and growth factors

Tests Based on Detoxification and Excretory Functions

1. Serum Bilirubin, a breakdown product of the porphyrin ring of heme-containing proteins, is found in the blood in two fractions—conjugated and unconjugated. The unconjugated fraction, also termed the *indirect fraction*, is insoluble in water and is bound to albumin in the blood. The conjugated (direct) bilirubin fraction is water soluble and can therefore be excreted by the kidney. When measured by the original van den Bergh method, the normal total serum bilirubin concentration is <17 micro mol/L (1 mg/dL). Up to 30%, or 5.1 micro mol/L (0.3 mg/dL), of the total is direct-reacting (or conjugated) bilirubin.

Elevation of the unconjugated fraction of bilirubin is rarely due to liver disease. An isolated elevation of unconjugated bilirubin is seen primarily in hemolytic disorders and in a number of genetic conditions such as Crigler-Najjar and Gilbert's syndromes .Isolated unconjugated hyperbilirubinemia (bilirubin elevated but <15% direct) should prompt a workup for hemolysis In the absence of hemolysis.

In contrast, conjugated hyperbilirubinemia almost always implies liver or biliary tract disease. The rate-limiting step in bilirubin metabolism is not conjugation of bilirubin, but rather the *transport of conjugated bilirubin into the bile canaliculi*. Thus, elevation of the conjugated fraction may be seen in any

type of liver disease. In most liver diseases, both conjugated and unconjugated fractions of the bilirubin tend to be elevated.

2. Serum Enzymes

The liver contains thousands of enzymes, some of which are also present in the serum in very low concentrations. These enzymes have no known function in the serum and behave like other serum proteins. They are distributed in the plasma and in interstitial fluid and have characteristic half-lives, usually measured in days. Very little is known about the catabolism of serum enzymes, although they are probably cleared by cells in the reticuloendothelial system. The elevation of a given enzyme activity in the serum is thought to primarily reflect its increased rate of entrance into serum from damaged liver cells.

Serum enzyme tests can be grouped into three categories: (1) enzymes whose elevation in serum reflects damage to hepatocytes, (2) enzymes whose elevation in serum reflects cholestasis, and (3) enzyme tests that do not fit precisely into either pattern.

A. Enzymes that Reflect Damage to Hepatocytes

The aminotransferases (transaminases) are sensitive indicators of liver cell injury and are most helpful in recognizing acute hepatocellular diseases such as hepatitis. They include the aspartate aminotransferase (AST) and the alanine aminotransferase (ALT). AST is found in the liver, cardiac muscle, skeletal

muscle, kidneys, brain, pancreas, lungs, leukocytes, and erythrocytes in decreasing order of concentration. ALT is found primarily in the liver. The aminotransferases are normally present in the serum in low concentrations. These enzymes are released into the blood in greater amounts when there is damage to the liver cell membrane resulting in increased permeability. Liver cell necrosis is not required for the release of the aminotransferases, and there is a poor correlation between the degree of liver cell damage and the level of the aminotransferases. Thus, the absolute elevation of the aminotransferases is of no prognostic significance in acute hepatocellular disorders.

Any type of liver cell injury can cause modest elevations in the serum aminotransferases. Levels of up to 300 U/L are nonspecific and may be found in any type of liver disorder. Minimal ALT elevations in asymptomatic blood donors rarely indicate severe liver disease; studies have shown that fatty liver disease is the most likely explanation. Striking elevations—i.e., aminotransferases > 1000 U/L—occur almost exclusively in disorders associated with extensive hepatocellular injury such as (1) viral hepatitis, (2) ischemic liver injury (prolonged hypotension or acute heart failure), or (3) toxin- or drug-induced liver injury.

The pattern of the aminotransferase elevation can be helpful diagnostically. In most acute hepatocellular disorders, the ALT is higher than or equal to the AST. An AST:ALT ratio > 2:1 is suggestive while a ratio > 3:1 is highly suggestive of

alcoholic liver disease. The AST in alcoholic liver disease is rarely >300 U/L and the ALT is often normal. A low level of ALT in the serum is due to an alcohol-induced deficiency of pyridoxal phosphate.

The aminotransferases are usually not greatly elevated in obstructive jaundice. One notable exception occurs during the acute phase of biliary obstruction caused by the passage of a gallstone into the common bile duct. In this setting, the aminotransferases can briefly be in the 1000–2000 U/L range. However, aminotransferase levels decrease quickly, and the liver function tests rapidly evolve into one typical of cholestasis.

B. Enzymes that Reflect Cholestasis

The activities of three enzymes—alkaline phosphatase, 5'-nucleotidase, and -glutamyl transpeptidase (GGT)—are usually elevated in cholestasis.

Elevation of liver-derived *alkaline phosphatase* is not totally specific for cholestasis, and a less than threefold elevation can be seen in almost any type of liver disease. Alkaline phosphatase elevations greater than four times normal occur primarily in patients with cholestatic liver disorders, infiltrative liver diseases such as cancer and amyloidosis, and bone conditions characterized by rapid bone turnover (e.g., Paget's disease). In bone diseases, the elevation is due to increased amounts of the bone isoenzymes. In liver diseases, the elevation is almost always due to increased amounts of the liver isoenzyme.

If an elevated serum alkaline phosphatase is the only abnormal finding in an apparently healthy person, or if the degree of elevation is higher than expected in the clinical setting, identification of the source of elevated isoenzymes is helpful. This problem can be approached in several ways. First, and most precise, is the fractionation of the alkaline phosphatase by electrophoresis.

The second approach is based on the observation that alkaline phosphatases from individual tissues differ in susceptibility to inactivation by heat. The finding of an elevated serum alkaline phosphatase level in a patient with a heat-stable fraction strongly suggests that the placenta or a tumor is the source of the elevated enzyme in serum. Susceptibility to inactivation by heat increases, respectively, for the intestinal, liver, and bone alkaline phosphatases, bone being by far the most sensitive

Tests that Measure Biosynthetic Function of the Liver

A. Serum Albumin: Serum albumin is synthesized exclusively by hepatocytes. Serum albumin has a long half-life: 18–20 days, with ~4% degraded per day. Because of this slow turnover, the serum albumin is not a good indicator of acute or mild hepatic dysfunction; only minimal changes in the serum albumin are seen in acute liver conditions such as viral hepatitis, drug-related hepatoxicity, and obstructive jaundice. In hepatitis, albumin levels < 3 g/dL should raise the possibility of chronic liver disease. Hypoalbuminemia is more common in

chronic liver disorders such as cirrhosis and usually reflects severe liver damage and decreased albumin synthesis. One exception is the patient with ascites in whom synthesis may be normal or even increased, but levels are low because of the increased volume of distribution. However, hypoalbuminemia is not specific for liver disease and may occur in protein malnutrition of any cause, as well as protein-losing enteropathies, nephrotic syndrome, and chronic infections that are associated with prolonged increases in levels of serum interleukin 1 and/or tumor necrosis factor, cytokines that inhibit albumin synthesis. Serum albumin should not be measured for screening in patients in whom there is no suspicion of liver disease.

B. Serum Globulins

Serum globulins are a group of proteins made up of Gamma globulins (immunoglobulins) produced by B lymphocytes and Alpha and Beta globulins produced primarily in hepatocytes. Gamma Globulins are increased in chronic liver disease, such as chronic hepatitis and cirrhosis. In cirrhosis, the increased serum gamma globulin concentration is due to the increased synthesis of antibodies, some of which are directed against intestinal bacteria. This occurs because the cirrhotic liver fails to clear bacterial antigens that normally reach the liver through the hepatic circulation.

Increases in the concentration of specific isotypes of Gamma globulins are often helpful in the recognition of certain chronic liver diseases. Diffuse polyclonal increases in IgG levels are common in autoimmune hepatitis; increases >100% should alert the clinician to this possibility. Increases in the IgM levels are common in primary biliary cirrhosis, while increases in the IgA levels occur in alcoholic liver disease.

C. Coagulation Factors

With the exception of factor VIII, the blood clotting factors are made exclusively in hepatocytes. Their serum half-lives are much shorter than albumin, ranging from 6 h for factor VII to 5 days for fibrinogen. Because of their rapid turnover, measurement of the clotting factors is the single best acute measure of hepatic synthetic function and helpful in both the diagnosis and assessing the prognosis of acute parenchymal liver disease. Useful for this purpose is the *serum prothrombin time*, which collectively measures factors II, V, VII, and X. Biosynthesis of factors II, VII, IX, and X depends on vitamin K. The prothrombin time may be elevated in hepatitis and cirrhosis as well as in disorders that lead to vitamin K deficiency such as obstructive jaundice or fat malabsorption of any kind.

CONGESTIVE CARDIAC FAILURE

Congestive cardiac failure is defined as inability of heart to maintain an output, at rest or during exercise, necessary for the metabolic needs of the body and inability to receive blood into ventricular cavity at low pressure during diastole.[18]

In our study, patients were included as having congestive cardiac failure, if they had at least one Major and Minor criteria of *Framingham criteria.* [19]

FRAMINGHAM CRITERIA

MAJOR

1. Paroxysmal nocturnal Dyspnea
2. Neck vein distension
3. Crackles
4. Cardiomegaly
5. Acute pulmonary edema
6. S3 gallop
7. Increased venous pressure (16cm H20)
8. Positive hepatojugular reflex

MINOR

1. Extremity edema
2. Night cough
3. Dyspnea on exertion
4. Hepatomegaly
5. Pleural effusion
6. Vital capacity reduced by one third to normal
7. Tachycardia > 120/ min
8. Weight loss over 4.5kg over 5 days treatment.

Heart failure may be described as systolic, diastolic, high output low output, acute or chronic and right or left sided. These separations blur in the course of the disease.

CAUSES OF CONGESTIVE CARDIAC FAILURE:[20]

Depressed Ejection Fraction (<40%)

Coronary artery disease

Nonischemic dilated cardiomyopathy

Myocardial infarction

Toxic/drug-induced damage

Myocardial ischemia

Infiltrative disorders

Chronic pressure overload/ Familial/genetic disorders

Hypertension

Metabolic disorder

Viral

Obstructive valvular disease

Chronic volume overload

Chagas' disease

Disorders of rate and rhythm

Intracardiac (left-to-right) shunting

Chronic bradyarrhythmias

Preserved Ejection Fraction (>40–50%)

Pathological hypertrophy

Restrictive cardiomyopathy

Primary(hypertrophic cardiomyopathy)

Infiltrative disorders (amyloidosis, sarcoidosis)

Secondary (hypertension)

Fibrosis

Aging

Storage diseases (hemochromatosis)

Pulmonary Heart Disease

Pulmonary vascular disorders

Cor pulmonale

High-Output States

Metabolic disorders

Excessive blood-flow requirements

Nutritional disorders (beriberi)

Chronic anemia

Systemic arteriovenous shunting

Thyrotoxicosis

Precipitating factors:

In evaluating heart failure, it is also important to identify precipitating factors. [21]

1. Anemia
2. Pregnancy
3. Infections
4. Thyrotoxicosis
5. Arrythmia
6. Infective endocarditis
7. systemic hypertension
8. metabolic and physical changes

Forms of heart failure:

Systolic Versus Diastolic Failure

This classification relates to whether the principal abnormality is the inability to contract normally and expel sufficient blood (systolic failure) or to relax and fill normally (diastolic failure). The major clinical manifestations of systolic failure relate to an inadequate cardiac output with weakness, fatigue, reduced exercise tolerance and other symptoms of hypoperfusion, while in diastolic failure they relate principally to an elevation of filling pressures. In many patients, abnormalities of contraction and relaxation coexist.

Diastolic heart failure may be caused by increased resistance to ventricular inflow and reduced ventricular diastolic capacity (constrictive pericarditis and restrictive, hypertensive, and hypertrophic cardiomyopathy), impaired ventricular relaxation (acute myocardial ischemia, hypertrophic cardiomyopathy), and myocardial fibrosis and infiltration.

High Output Versus Low Output Heart Failure

Low output heart failure occurs secondary to ischemic heart disease, hypertension, dilated cardiomyopathy, and valvular and pericardial disease. High output heart failure occurs in hyperthyroidism, anemia, pregnancy, arteriovenous fistulas, beriberi, and Paget’s disease.

Acute Versus Chronic Heart Failure

The prototype of acute heart failure is the patient who is entirely well but who suddenly develops a large myocardial infarction or rupture of a cardiac valve. Chronic heart failure is typically observed in patients with dilated cardiomyopathy or multivalvular heart disease that develops or progresses slowly. Acute heart failure is usually largely systolic and the sudden reduction in cardiac output often results in systemic hypotension without peripheral edema. In chronic heart failure, arterial pressure tends to be well maintained until very late in the course, but there is often accumulation of peripheral edema.

Right Sided Versus Left Sided Heart Failure

Patients in whom the left ventricle is mechanically overloaded (e.g., aortic stenosis) or weakened (e.g., post myocardial infarction) develop dyspnea and orthopnea as a result of pulmonary congestion, a condition referred to as left sided heart failure. In contrast, when the underlying abnormality affects the right ventricle primarily (e.g., pulmonic stenosis or pulmonary hypertension), symptoms resulting from pulmonary congestion are less common, and edema, congestive hepatomegaly, and systemic venous distention, are more prominent. However, when heart failure has existed for months or years, biventricular failure usually results. For example, patients with long standing aortic valve disease or systemic hypertension may have ankle

edema, congestive hepatomegaly, and systemic venous distention late in the course of their disease.

Backward Versus Forward Heart Failure

The concept of backward heart failure contends that in heart failure, one or the other ventricle fails to discharge its contents or fails to fill normally. As a consequence, the pressures in the atrium and venous system behind the failing ventricle rise, and retention of sodium and water occurs as a consequence of the elevation of systemic venous and capillary pressures and the resultant transudation of fluids into the interstitial space. In forward failure, salt and water retention is a consequence of diminished renal perfusion and excessive proximal tubular sodium re-absorption and of excessive distal tubular re-absorption through activation of the renin-angiotensin-aldosterone system.

Irrespective of the type of failure, Congestive heart failure affects liver structurally and various functions of liver.

In this study, changes in liver function tests in various causes of congestive cardiac failure such as rheumatic, congenital, ischemic, cardiomyopathic, cor pulmonale and hypertensive heart diseases are noted in 75 patients presenting with heart failure and compared with themselves and a control of 20 apparently healthy individuals. Also, the patients are tracked for 7 days, liver function tests

are performed again and compared with admission values, to note whether remission or exacerbation has any impact on LFTs.

Review of other Studies and journals:

One of the most common manifestations of congestive heart failure is enlargement of the liver. This fact has led several investigators such as *Jollife; Robertson* [1] [2] [3] [4] to study liver function tests in an attempt to evaluate hepatic dysfunction in congestive heart failure.

Historically, the first association of liver pathology and congestive heart failure was noted by *Kiernan* [6] who described the "nutmeg liver." Seventy eight years later *Mallory* [7] described the typical microscopic appearance of central congestion with focal necrosis. Other authors pointed out the fatty changes [8] and the compression of capillaries by edema fluid accumulated between the liver cell cords and capillaries [9] [10].

The three main theories of the pathogenesis of the altered liver anatomy are: **infection,[7]. mechanical compression [11] [12] and hypoxia with secondary nutritional deficiency [13] [14] [15]** The deficiency in oxygen supply to liver cells in heart failure seems to be due not only to the slowing of blood flow through the liver but even more so to arterial unsaturation resulting from pulmonary lesions. This was stressed by *Rich* [14] and others [13] [22] [15] who pointed out that the jaundice of heart failure is especially apt to develop following pulmonary infarction. *Ingelfinger's* [23] studies of bromsulfalein

removal rates by means of hepatic vein catheterization, and the studies of blood flow to other organs in congestive heart failure'5' 16, 67, 68, 71, 97 make it reasonable to assume that there is a decrease in blood flow to the liver in the presence of cardiac decompensation.

From the Medical Division of the Montefiore Hospital, there is other evidence for impaired liver function in congestive heart failure. Hepatic fibrosis has been found three times as great in patients with heart failure as in patients without heart failure.[24] [35] [26]. More significantly, central fibrosis so common in decompensated cardiac patients, did not occur at all in patients who were not in heart failure.

Hyperbilirubinemia has been found in patients who were in severe chronic heart failure. *Jolliffe*[37] and *Cantarow*[6] noted that bromsulfalein was not cleared from the blood at a normal rate in the presence of heart failure. Blood cholesterol levels do not seem to be altered by circulatory embarrassment.[40] *Gravin* [25] in 1943 observed 35 cases of cardiac cirrhosis in 790 autopsy cases in whom heart failure was chief cause of death.The consensus is that there is a severe aberration in liver function in association with a failing heart.

*S.Sherlock[*43] described the clinical and biochemical features of zone 3 necrosis in patients with heart failure.

Killip T. Payne in 1960 [38] described massive elevation of serum transaminases level secondary to cardiogenic shock.

Mechanism of liver injury in congestive cardiac failure:

Congestive heart failure causes:

1. Decreased hepatic blood flow
2. Increased hepatic venous pressure leading to edema of the sinusoids and atrophy of hepatocytes.
3. Decreased arterial saturation which could result in hepatocellular hypoxia.[39]

Single most important factor is Hypoxia of liver cells resulting in centrilobular necrosis (zone3).[44] Also ,in heart failure passive congestion of liver results due to increased venous pressure transmitted to small hepatic veins that drain Acini[42].

Microscopic studies reveled increased pressure can cause atrophy zone 3 hepatocytes.[45]. In addition, elevated venous pressure results in sinusoidal congestion enlargement of sinusoidal fenestrae , through which protein rich fluid then enters into the space of disse. [50]. The resulting perisinusoidal edema may impair diffusion of oxygen and nutrients into the hepatocytes.[45]

Excess fluid in the space of disse normally drains into hepatic lymphatics, but when lymph formation exceeds the capacity of the lymphatics, high protein fluid exudes from the surface of the liver into the peritoneal cavity and the typical high protein ascities of heart failure develops [51].

In the chronic hepatic congestion, fibrosis may develop in perivenular area ,zone 3 and space of disse and further impair the diffusion of oxygen and nutrients from blood to hepatocytes. The fibrosis varies from one region of the liver to the other. This variability may be partly explained by the fibrogenic effects of focal thrombi within the sinusoidal hepatic venules and portal veins that are a consequence of chronic vascular stasis [47].

Passive congestion alone does not seem to be sufficient to cause significant hepatic necrosis, decreased hepatic blood flow is also necessary [42]. This conclusion is supported by the observation of S.Sherlock [43], of the lack of correlation between right atrial pressure and the degree of zone 3 necrosis in patients with congestive heart failure. Moreover, significant zone 3 necrosis caused by acute left sided heart failure has been documented in the complete absence of right sided heart failure, a finding that suggests cardiac output is the principal determinant of hepatic ischemia [47]. However passive congestion seems to be an important co factor in most cases of clinical apparent hepatic ischemia. In a recent study all patients with the clinical diagnosis of ischemic hepatitis were found to have clinically significant cardiac disease and 94% have right sided heart failure [48].

In another study, ischemic hepatitis in patients with chronic respiratory disease and patients with congestive heart failure, all but one patient

with ischemic hepatitis had a central venous pressure above 10 cmH20.[49]. These findings suggests that chronic passive congestion major role in sensitizing the liver to hemodynamic and hypoxic insults

Hepatic ischemia:

Hepatic ischemia like ischemia involving other organs results from the imbalance between hepatic oxygen supply and demand. Because of the metabolic rate of the liver is relatively constant, oxygen supply, not demand is principal determinant of hepatic ischemia [52]. Hepatic oxygen delivery is the function of both the oxygen content of the blood and total hepatic blood flow.

Systemic hypoxia alone is usually insufficient to cause significant Hepatic injury [53][54],but severe hypoxemia was reported to cause hepatic injury in a patient with obstructive sleep apnea[55]
And in a series of patients with exacerbation of chronic respiratory failure usually, in the setting of passive hepatic congestion resulting from right sided heart failure.[49].

Most critical factor in hepatic ischemia is total hepatic blood flow. Numerous studies have shown that hepatic blood flow is determined primarily by cardiac output and that the splanchnic bed receives relatively constant 25% of the cardiac output [56] The liver has a dual blood supply receiving about 17 – 34%

of the blood flow from the hepatic artery and 66 – 83 % via the low pressure portal vein, in which the oxygen saturation is relatively high [57] [58], thus much of its oxygen supply from the portal vein.

If patients cannot increasse their cardiac output there is a fall in splanchnic blood flow with exercise and a reduced hepatic blood flow, the oxygen requirement of the liver does not change and the oxygen extraction increases[56] [59]. In the resting state, increased extraction of oxygen by hepatocytes compensates for the reduction of hepatic blood flow. However, under situations of systemic stress, such as sepsis or increased physical activity in which the cardiac output cannot increased to supply extra hepatic metabolic demands and the hepatic and splanchnic perfusion falls. Hepatic oxygen extraction is often unable to increase above an already elevated baseline, and hepatocellular hypoxia results, especially in zone3 of the hepatic acini.[51].

Data from in vitro and animal models suggest that because of their high metabolic rate, hepatocytes are vulnerable to hypoxia at physiological temperatures than other cell types in liver such as kupffer cells, sinusoidal endothelial cells and biliary epithelial cells.[60]

Furthermore, nutritional status has an important influence on hepatic cellular sensitivity to hypoxia. Fasted rats appear less prone than fed rats to

hepatic ischemia, possibly because their diminished glycogen stores provides less substrate for anaerobic glycolysis, so that the intra cellular production of lactic acid is decreased.[61]. The cellular mechanism of ischemic injury, which occurs when hepatocytes injured appears to be related to a disruption of mitochondrial respiration, depletion of adenosine triphosphate rise in levels of intracellular calcium and activation of cellular proteases.[62] [66]

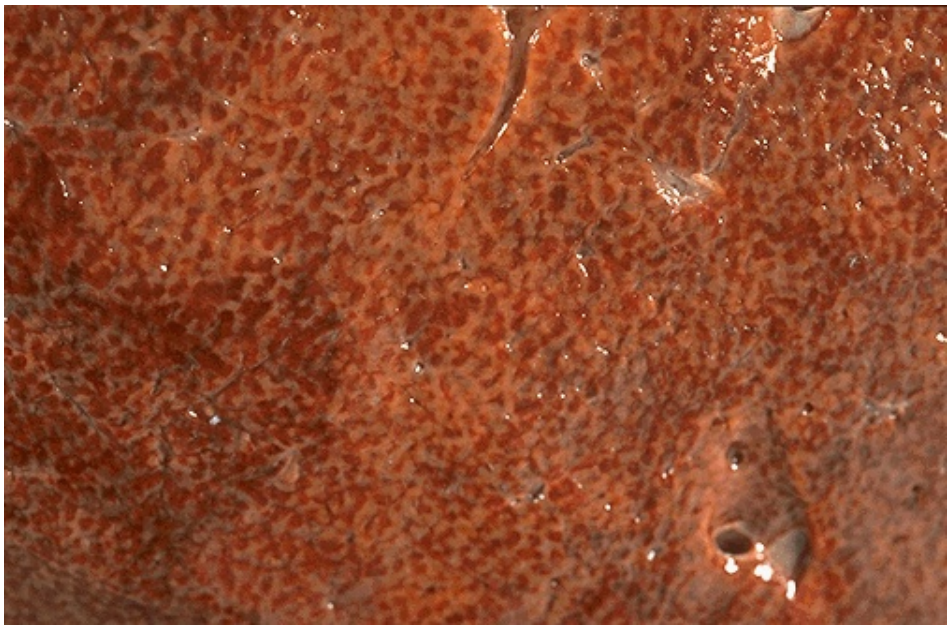
Further contributing hepatic damage under these conditions is reperfusion injury which occurs when hepatocytes injured by ischemia are exposed to oxygen. Reperfusion injury is mediated by generation of free radicals, causing injury through lipid peroxidation.[60]

Within injured hepatocytes, mitochondria generate toxic oxygen species from reduced electron carriers. In addition, ischemia promotes the conversion of cytosolic xanthine dehydrogenase to xanthine oxidase which results in turn in production of superoxide and hydrogen peroxide from accumulated xanthine.[63]. In addition to the direct toxic effects of reactive oxygen species, ischemia and reperfusion induce the transcription of multiple genes in the hepatocytes via transcription factors, heat shock factor and nuclear factors, the product of these genes, including various cytokines, may contribute to hepato cellular injury [64].

PATHOLOGY OF LIVER IN CONGESTIVE CARDIAC FAILURE

Macroscopic features:

The liver in congestive heart failure is enlarged and purple in colour with rounded edges. At autopsy, a cut section usually shows the nutmeg appearance associated with venous distension [43]; regular deep brown centrilobular zones alternating yellow or pale tan periportal zones. When cardiac sclerosis is present, the capsular surface is pitted and granular, on the cut surface; poorly circumscribed areas of parenchymal granularity or nodularity emerge from periportal zones, the nodules being less than 1-2mm in diameter. This picture differs from true cirrhosis because of the very small size of nodules, their non uniform distribution, poor circumscription and their origin from periportal regions.



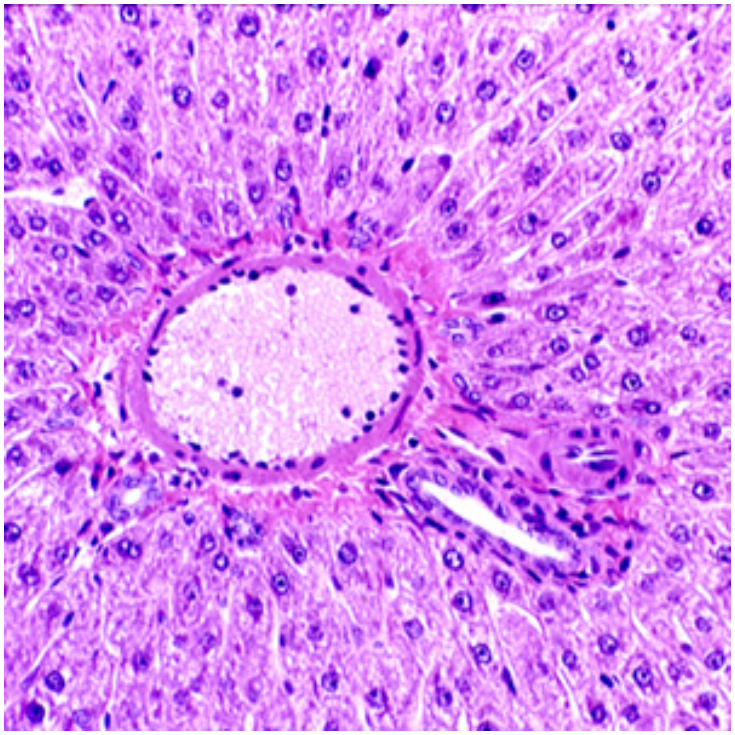
a "nutmeg" liver seen with chronic passive congestion of the liver

Microscopic features:

Heart failure may cause the histological changes of passive congestion and centrilobular necrosis but hepatic morphology may be normal. In a study presented in American heart journal, among 75 patients with liver failure, 47 had normal liver biopsy [67]. With mild congestion due to an elevated venous pressure, centrilobular hepatocytes become compressed and atrophic and the adjacent sinusoids are engorged with blood.

If there has not been severe or chronic congestion, little else is seen [68]. With increasing congestion more marked hepatocellular compression with atrophy is seen wit an extension further from the central veins. Increased brown pigment in the centrilobular liver cells is a consistent finding.

With increasing congestion centrilobular necrosis increases and fibrosis develops bridging central veins [70]. However, centrilobular necrosis can occur in severe heart failure without hypotension or shock [71] suggesting that it is a low cardiac output, causing decreased blood flow and parenchymal hypoxia which is main prerequisite for centrilobular necrosis.[72]. Shock is an extreme form of low cardiac output state.



NORMAL LIVER

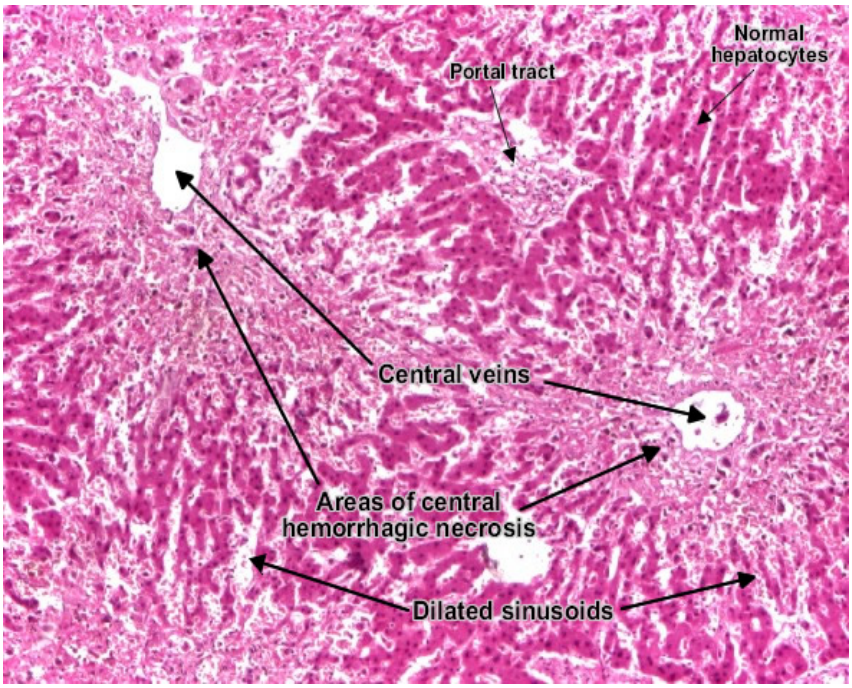
Centrilobular necrosis in Heart failure may be associated with an inflammatory reaction consisting of polymorphonuclear leukocytes or lymphocytes and plasma cells, and this picture may depend on the duration of ischemia. Cardiac sclerosis consists of fibrosis of central veins and at the centrilobular region, with or without bridging to other central veins or portal tracts. In one study cardiac sclerosis was the most common form of hepatic fibrosis, occurring in 48% of the cases[79].

Regenerative hyperplasia may be seen in peripheral zones, the parenchyma showing a variable increase in the number of hepatocytes within the liver cell plates. In most cases plate thickening alone, “Twinning” of liver cells occur, with three to five cells forming the plates. Affected cells are often enlarged

with a pale cytoplasm and enlarged and pleomorphic nuclei. Nodular regenerative hyperplasia has been found in a small number of cases.

Cardiac cirrhosis appears to be relatively uncommon and can be considered as a progression from cardiac cirrhosis. Central- central and central-portal fibrosis and fibrous scars adjacent to parenchyma showing early nodularity, are the main histological findings.

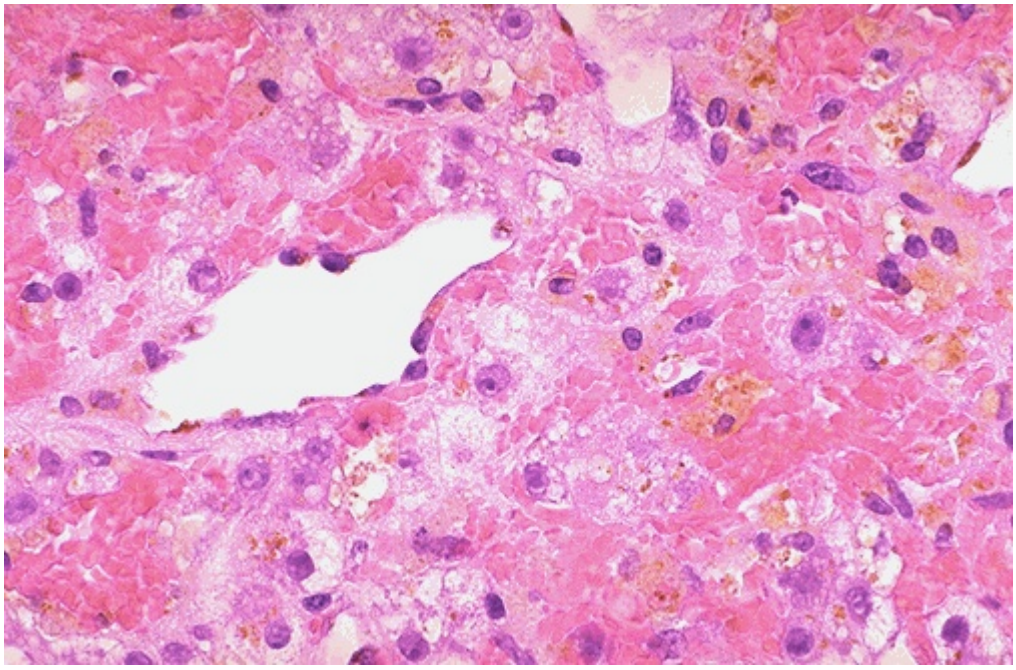
Passive congestion (Passive hyperemia) (liver).



Passive congestion of the liver. (H&E, ob. x10)

Passive congestion of the liver. Central veins, spaces of Disse and central vascular sinusoids are dilated, compressing the hepatocytes which are atrophied and, with progression, will necrotize - central hemorrhagic necrosis (compression and/or ischemic mechanism). Mediolobular

hepatocytes may present *fatty change* (hypoxic mechanism); periportal hepatocytes are normal



If the passive congestion is pronounced, then there can be centrilobular necrosis, because the oxygenation in zone 3 of the hepatic lobule is not great. The light brown pigment seen here in the necrotic hepatocytes around the central vein is lipochrome.

Congestive hepatopathy is characterized by:

- Perisinusoidal fibrosis,
- Hepatic venule dilation, and
- Dilation of the sinusoids in zone III (centrilobular)

Clinical Features of congestive liver disease:

In the mid of 20th century the leading cause of congestive cardiac failure leading to liver dysfunction was Rheumatic heart disease [67][68], especially, mitral stenosis and tricuspid regurgitation. In the industrial world it is the atherosclerotic heart disease the most common cause. Hypertensive heart disease is also on the rise. Other causes are as dilated/ Restrictive cardiomyopathy congenital heart disease and corpulmonale.

Liver dysfunction in congestive heart failure is usually mild and asymptomatic and often detected incidentally on routine liver biochemical investigations. The clinical presentation arises mainly from the cardiac disease. Some patients may experience right upper quadrant pain secondary to stretching of hepatic capsule from an enlarged liver. This symptom may be present in acute right- sided heart failure or with exacerbation of chronic heart failure. Anorexia, nausea and vomiting may also occur, but it is unclear whether they are caused by hepatic congestion, intestinal congestion or other factors such as medication, hypoxia or shock.[51].

Heart failure is rare but reported cause of hepatic encephalopathy and coma[67] and hepatic congestion can also cause severe hypoglycemia, which may induce stupor[74][75]. Fulminant hepatic failure may result from previously unrecognized cardiomyopathy and treatment of heart condition may improve liver failure.[76]

On physical examination jaundice is present in approximately 20% of patients with congestive liver disease and is dependent on severity of heart failure [68]. Of interest, edematous tissue do not appear jaundiced because bilirubin is protein bound, and therefore does not enter the edematous areas which have a low protein content [77].

Hepatomegaly occurs in 95-99% of patients with moderate to severe right heart failure [51][67]. The enlarged liver may be palpated 5 cms below costal margin in as many as 50% of patients [73].

Hepatojugular reflex can be elicited by applying manual pressure over the liver, which increases venous return to the heart. Because the already impaired right heart is unable to accommodate the increased blood flow, the resultant back pressure is transmitted to the jugular vein, which is visible on physical examination. In the presence of tricuspid regurgitation, a pulsatile liver can be palpated. This is the result of transmission of back pressure from the regurgitant flow from the hepatic veins [51]. Other etiologies of hepatic pulsation in the right sided heart failure include cor-pulmonale and constrictive pericarditis.

Peripheral edema is seen in 70-77% of patients with right sided failure, pleural effusion in 12-25% of patients but can be as high as 79% in patients with cardiac cirrhosis. [51,73] . Ascites is reported in 7 – 49%of patients [67][73]. In cardiac ascites protein concentration is usually >2.5g/dl and serum ascitic albumin gradient is < 1.1g/dl.[78]

CAUSES OF CARDIAC FAILURE

Causes of cardiac failure in studies conducted by 2 physicians; in the study of liver function abnormalities.

ETIOLOGY	**White et al**		**Richman et al**	
	No. of patients	**Percentage (%)**	**No. of patients**	**Percentage (%)**
Atheroscelerotic HD	12	16	58	33.1
Hypertensive HD	23	30.7	38	21.7
Rheumatic HD	33	44.7	56	32
Cor pulmonale	2	2.7	10	5.7
Constrictive pericarditis	2	2.7	7	4.0
Others				
Congenital			3	1.7
Syphilitic	1	1.3	1	0.6
Scleroderma			1	0.6
Thyroid	2	2.7		
Ball valve thrombosis			1	0.6
TOTAL	75	100	175	100

LIVER FUNCTION TESTS IN CARDIAC FAILURE:

SERUM BILIRUBIN:

Congestive heart failure results in abroad range of liver biochemical abnormalities. The most common is a mild increase in serum bilirubin levels, which occurs inn about 70% of patients [51]. The total serum bilirubin is usually less than 3mg/dl with a high unconjugated fraction [51]. However strikinglyhyperbilirubinemia may develop in patients with severe usually acute right sided heart failure.The exact mechanism of hyperbilirubinemia is unclear and multiple factors are thought to contribute,including hepatocellular dysfunction, hemolysis,pulmonary infarction secondary to distented hepatic veins,medications,superimposed sepsis.

S. Sherlock [43] found a correlation of the serum bilirubin level with right atrial pressure,not the cardiac output.Therefore,the jaundice of the right sided heart failure seems to be clinically and pathophysiologically distinct from that associated ischaemic hepatitis and results from congestion rather than diminished hepatic perfusion.Upon improvement of the right sided heart failure elevated serum bilirubin levels return back to normal quite rapidly over a period of 3 to 7 days.

SERUM AMINOTRANSFERASES:

Serum aminotransferases, glutamate dehydrogenase, lactic dehydrogenase are all elevated in right sided heart failure [80,73]. Asparate transaminase, alanine transaminase rise in up to a third of patients and show, similar increases, an increased lactate dehydrogenase is found in 20 to 60% of patients.

In a series of 175 patients with acute and chronic heart failure [73] asparate transaminase was elevated in 49% of those with acute heart failure, but only in 5% of those with chronic heart failure;80% of the high levels were between 40 and 80 I.U. Alanine transaminase results paralleled, but were less marked than, those of asparate transaminase. Very high values of asparate transaminase (1000-10,000I.U) can occur with an acute onset of severe heart failure especially if it is associated with hypotension or shock [43, 72] and they correlate well with the degree of centrilobular hepatic necrosis.

Increased venous congestion and decreased hepatic perfusion both contribute to the elevation of aminotransferases, although centrilobular hypoxia and or necrosis are probably the major factors.

The increase in asparate transaminase and alanine transaminase and lactate dehydrogenase correlate with increase in systemic venous pressure, pulmonary capillary wedge pressure and cardiac index, but the

correlation coefficients are low suggesting that other factors must also be involved [80]

Very high enzyme levels in congestive heart failure are often misinterpreted as evidence of viral or drug induced hepatitis [81].The following clinical features suggest that circulatory failure is the cause of liver cell necrosis [82].

I. The presence of chronic heart failure

II. A recent episode of acute circulatory failure

III. The early appearance of renal insufficiency(this tends to be a late development in severe viral hepatitis)

SERUM ALKALINE PHOSPHATASE

Serum alkaline phosphatase rises by about 10-20% in patients with congestive cardiac failure [43, 51,73]. However in most patients the levels are within normal limits; rarely do they exceed twice normal. Elevation in serum alkaline phosphatase levels do not correlate with increases in serum bilirubin or aminotrnsferases. The highest elevations are usually seen in patients with marked liver enlargement. The etiology of abnormal serum level, therefore is thought to be a result of intra hepatic obstruction secondary to hepatic congestion.[73] . With the improvements in cardiac status, serum alkaline phosphatase returns to normal in approximately one week.

PROTHROMBIN TIME:

The prothrombin time is prolonged in 80 – 90% of patients with congestive cardiac failure with congestive hepatomegaly and is therefore a sensitive index of right-sided heart failure [43,67,73]. Parenteral administration of vitamin k results in little or no correction, suggesting that decreased hepatic synthesis or decreased activation of vitamin k dependent clotting factors may play a role.[67, 73]. Resolution of the prolonged prothrombin time usually takes 2-3 weeks after successful treatment of the right sided heart failure. Caution should therefore be exercised when treating patients in heart patients with warfarin or coumarin derivatives [83].

SERUM PROTEINS:

Serum albumin is low in about 30-50% of patients with congestive hepatomegaly [51, 73]. And the incidence and degree of change appears to be similar in acute and chronic failure. The changes were not marked, in 75% of those with reduced albumin the values were between 2.5- 2.9gm/dl. The lowest values were in patients with right- sided pressures due to rheumatic heart disease or cor pulmonale.

Serum albumin concentrations below 1.5 gm/dl are rarely observed and are often associated with marked ascites and edema. The etiologies of hypoalbuminea in heart failure include impaired hepatic synthesis, leakage or

decreased absorption from the congested intestine and poor nutrition. With the resolution of underlying cardiac disease, improvement in serum levels usually occurs over a period of few months. The serum albumin levels do not correlate with the degree of biological damage to the liver.

Hyperglobulinemia occurs in 37- 60% of patients with the right- sided heart failure, and is more common in patient with acute than with chronic heart failure[73]. The elevations tend to be mild with levels between 3.5 and 4.1 g/dl in the majority of patients. In contrast to other liver tests, the hyperglobuminemia usually does not return to normal after treatment of congestive heart failure.

Prolonged or recurrent episodes of congestive heart disease can lead to cardiac cirrhosis. The incidence is rare, however, most patients die of the underlying disease before cirrhosis can develop.

MATERIALS AND METHODS

All cases of congestive cardiac failure (75), of varied etiologies observed in patients from july 2008 - december 2009. 20 healthy individuals were taken as controls. Liver function tests are performed to both controls and cases, serum bilirubin, AST, ALT, SAP, Serum proteins and Prothrombin time admitted at Govt. Royapettah Hospital during the period from july 2008 to both on day 1 and day 7 of admission.

This study is an observational study, comparing the liver functions between cases (various causes of heart failure) and between cases and controls.

Cases:

Heart failure patients due various etiologies including Coronary heart disease, rheumatic heart disease, hypertensive heart disease, cor pulmonale and cardiomyopathy meeting the following inclusion criteria and not possessing following exclusion criteria were selected

INCLUSION CRITERIA

1. Cases of congestive cardiac failure, as per Framingham criteria; of various age groups and etiologies such as

- Rheumatic valvular Heart Disease
- Ischemic Heart Disease
- Hypertensive Heart Disease
- Congenital Heart Disease

- Cardiomyopathies
- Corpulmonale

2. Congestive cardiac failure of varied presentation either acute or chronic.

EXCLUSION CRITERIA

1. Known alcoholic
2. Past History of jaundice
3. Recent intake of Hepatotoxic drugs or drugs causing raised liver parameters, such as Rifampicin, INH, Steroids, chlorpromazine, amiadarone, statins, hydralazine , phenytoin and valproate.
4. positive viral markers

Controls:

Healthy individuals between 20-60 yrs of age without any known history of medical illness such as heart and liver diseases were selected.

Consent:

The study groups thus identified were instructed about the nature of the study. Willing participants were taken up after getting a written informed consent from them

In this study the following liver functions tests were done:

1. Serum bilirubin
2. serum transaminases
3. serum alkaline phosphatase
4. serum proteins
5. prothrombin time.

Results were entered in Microsoft Excel Spreadsheet and analyzed. Significance values were analyzed using **Minitab software, Epi.info software**. Chi- square test, Student 't' values was applied for significance. Significance was considered, if the 'p' value was below 0.05.

SERUM BILIRUBIN

Serum bilirubin was estimated by the vanden bergh reaction. In this reaction the bilirubin pigments are diazotized by sulphalinic acid and the chromatographic products are measured calorimetrically. Vanden bergh reaction can be used to distinguish between conjugated and unconjugated bilirubin because of the different solubility properties of the pigments. When the reaction is carried out in an aqueous medium, the water soluble conjugated bilirubin reacts to give the direct van den Bergh reaction. When the reaction is carried out in ethanol, the intramolecular hydrogen bonds of unconjugated bilirubin are broken. Thus both conjugated and unconjugated pigments react giving the total bilirubin level. The total minus direct reacting bilirubin gives the indirect value which is the measure of unconjugated bilirubin level

SERUM ENZYME ASSAYS

A number of serum enzymes have been used to distinguish and assess the cellular injury and biliary tract dysfunction or obstruction. All have limitations in sensitivity and specificity and not truly distinguished the processes definitely. Elevations in enzyme activities may be hepatic as well as non hepatic disorders like circulatory failure. With and careful interpretation, a number of serum enzymes provide important clinical tools.

In this study, the serum enzymes namely SGOT and SGPT was done by enzymatic substrate method. The substrate used are SGOT and SGPT substrate respectively along with D,N,P,H Di nitro-phenyl hydrannel

Principle:

These enzyme catalyse the transfer of the gamma amino groups and alanine respectively to the gamma keto group of keto glutamase to the formation of oxalo acetic acid and pyruvic acid.

SERUM ALKALINE PHOSPHATASE

Human serum contains several forms of alkaline phosphataseA plasma membrane derived enzyme of uncertain physiologic function Which hydrolyses acetic phosphate enters at pH 9. A number of different assays have been developed which utilize different substrates. Here the

substrate used were Amino-antipyrine solution, potassium ferri cyanide, alkaline phosphate buffer and substrate. Elevated levels of

alkaline phosphatase activity usually reflect impaired biliary tract function. The Increased levels reflect increased synthesis of the enzyme by hepatocytes and biliary tract epithelium rather than restoration of the enzyme due to obstruction. Slight to moderate increased alkaline phosphatase activity can occur secondary to congestive cardiac failure.

SERUM PROTEINS

Extensive liver injury may lead to decreased blood levels of

albumin, fibrinnogen, prothrombin, and other proteins synthesized exclusively by hepayocytes. In contrast to serum enzymes measurements serum protein level estimation reflect liver synthetic function rather than hepatocellular injury. Some proteins are neither early nor sensitive indicators of liver disease, because of the extent of hepatic reserve and their half life. Serum albumin is quantitatively the most important serum protein synthesized by the liver. The normal value ranges from 3.5 – 5.5 mg/dl. Albumin has a fairly long half life [14 -20 days] with less than 5% turnover daily. It is therefore not a good indicator of acute or mild liver injury.

Serum globulins are a heterogeneous group of proteins, normally 2.0 – 3.5 mg /dl includes alpha and beta globulins as well as serum immunoglobulins. Varying degree of hyperglobulinaemia reflect increased stimulation of the

periphery reticulo-endothelial compartment due to shunting of antigens passed the liver and impaired clearance by hepatic kupffer cells.

Serum proteins were estimated by the Biuret method. In this substances which contain two CO –NH2 groups joined together directly or through a single carbon nitrogen atom and those which contain two or more peptide links give a blue or purple colored compound with alkaline copper solution. The amount of colour given by the biuret reaction also varies appreciably for different proteins.

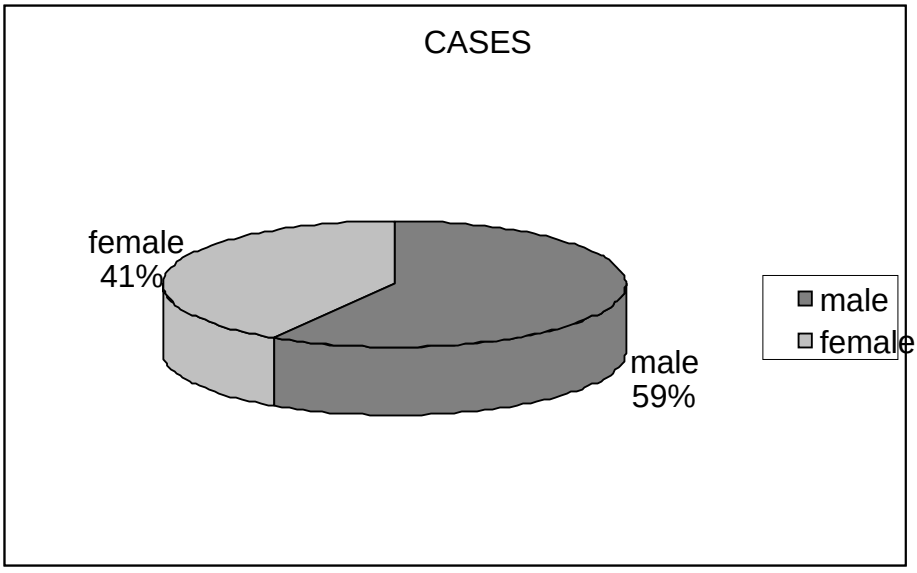
PROTHROMBIN TIME

Liver synthesizes six coagulation factors namely Fibrinogen [Factor– Prothrombin(Factor–II) and Factors V,VII,IX,X. Abnormalities of these coagulation factors can be most efficiently determined by the one stage prothrombin time which measures the rate of prothrombin conversion to thrombin in the presence of thromboplastin and calcium and requires the integrity of vitamin K dependent coagulation factors. The prothrombin time is dependent on normal hepatic synthesis of clotting factors and sufficient intestinal uptake of vitamin K. Acute or chronic parenchymal liver injury may lead to prolongation of the prothrombin time due to impaired synthesis of clotting proteins, because these proteins have a shorter half life, the prothrombin time may be regarded as an earlier indicator of severe liver injury and its elevation in both acute or chronic hepatocellular injury serves as an ominous prognostic sign.

RESULTS

Table 1 – Sex distribution of cases and controls

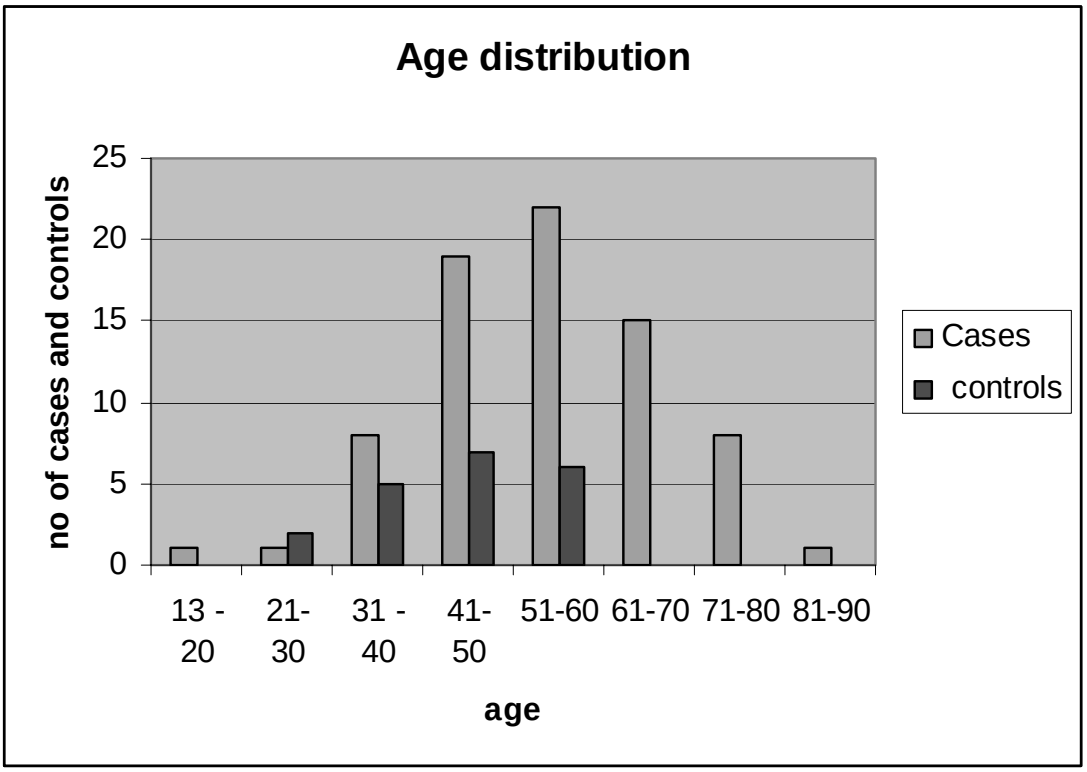
	controls	cases
Total	20	74
Male	12	44
Female	8	31
ratio	1.5:1	1.4:1



p value is not significant – 0.914

Table -2 Age distribution of cases and controls

Age group	Cases			Controls		
	Total	male	female	Total	male	female
13 -20	1	1	0	0	0	0
21- 30	1	0	1	2	2	0
31 -40	8	3	5	5	2	3
41- 50	19	9	10	7	4	3
51-60	22	17	5	6	4	2
61-70	15	9	6	0	0	0
71-80	8	4	4	0	0	0
81-100	1	1	0	0	0	0
total	75	44	31	20	12	8



p value insignificant: 0.0644

Table 3-

Duration of illness

Years of Heart failure	No of cases	percentage
< 1yr	4	5.3%
1-5 yrs	33	44%
>5 yrs	38	50.6%

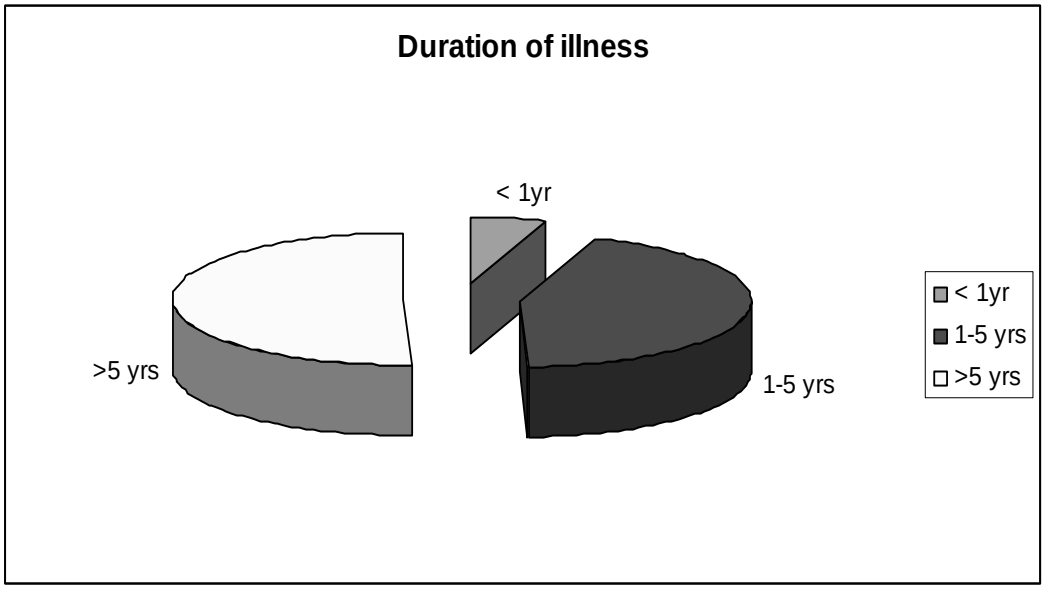


Table – 4

Etiology of heart failure

Etiology	No of cases	Percentage
Rheumatic heart disease	18	24%
Coronary heart disease	30	40%
Cor pulmonale	13	17.3%
cardiomyopathy	7	9.3%
Hypertensive heart disease	7	9.3%

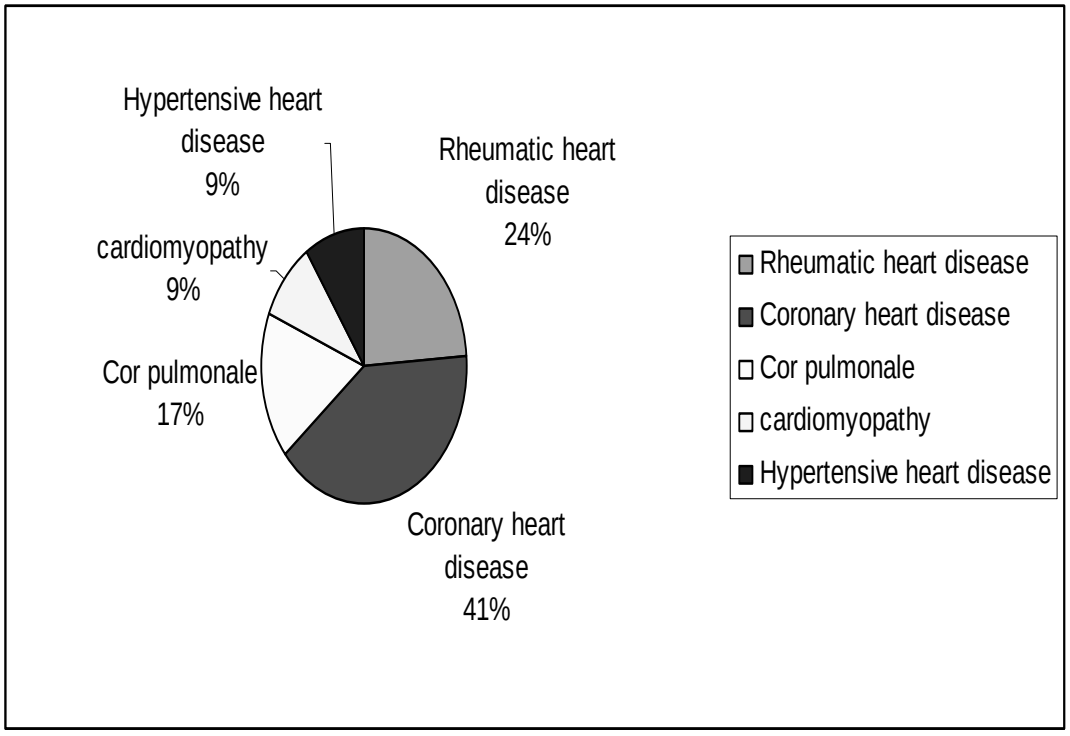
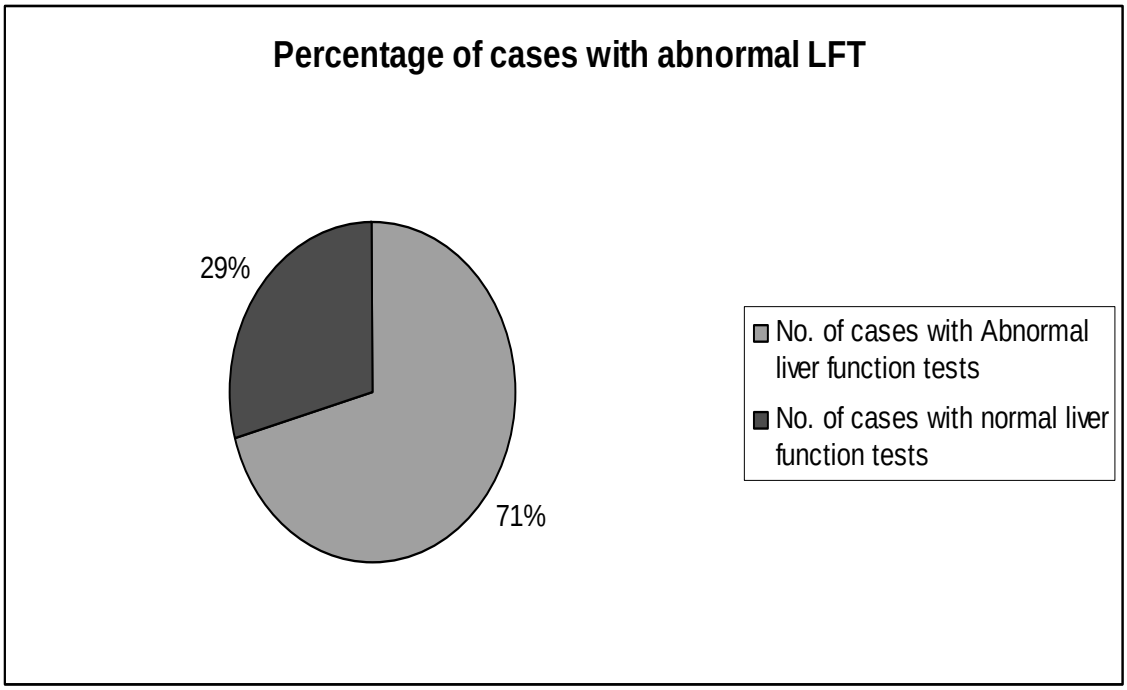


Table 5

Percentage of abnormal liver function tests

	Cases	controls
total	75	20
No. with abnormal liver function tests	53	0
Percentage with abnormal liver function tests	70.6%	0%



p value significant – 0.0003.

Table 6

Abnormal liver function tests as per etiology

ETIOLOGY	No. of cases	No. of cases with abnormal liver function tests	Percentage
Rheumatic heart disease	18	13	72%
Coronary Atherosclerotic heart disease	30	22	73%
Cor pulmonale	13	9	69%
Cardiomyopathy	7	5	71%
Hypertensive heart disease	7	4	57%

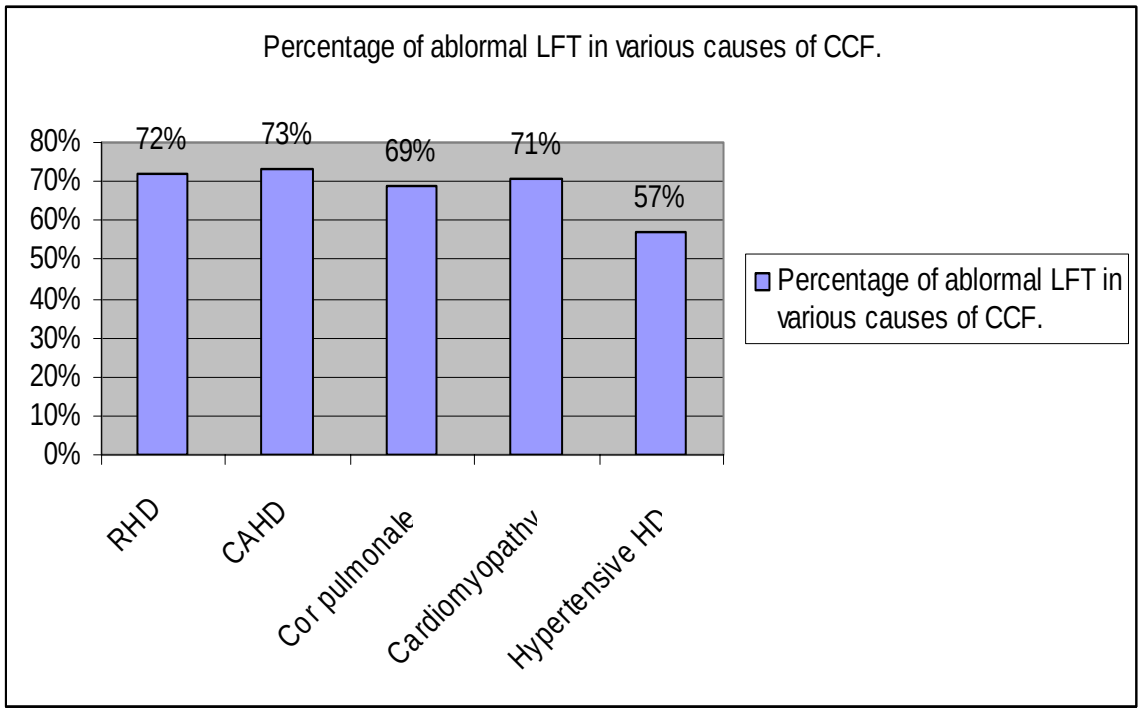


Table 7

Clinical Jaundice

Total no of cases	75
Cases with clinical jaundice	16
Percentage of clinical jaundice	21%
Controls	None showed jaundice

Table 8

Ascites

Total no cases	75
Cases with ascites	6
Percentage	8%
Controls	Nil

Table 9

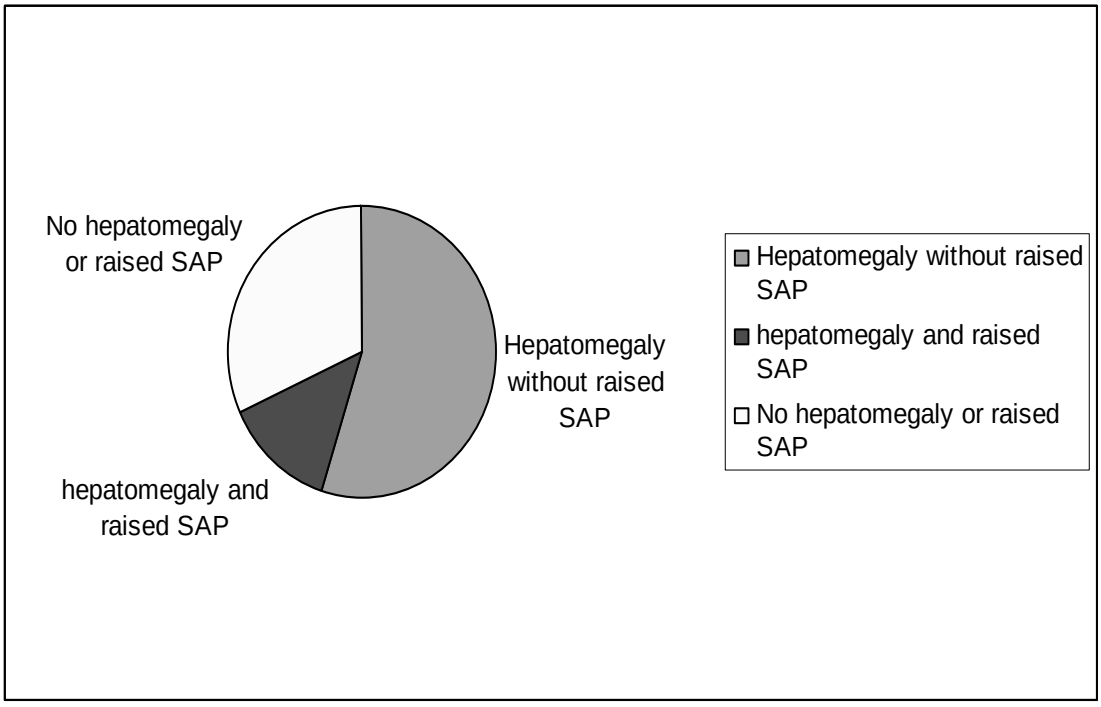
Hepatomegaly

Total no cases	75
No of cases with hepatomegaly	51
Percentage	68%
Controls	0 out of 20 showed hepatomegaly

Table 10

No of cases with hepatomegaly showing increased serum alkaline phosphatase

No of Cases with Hepatomegaly	51 (out of 75)
Cases with raised SAP	10 (out of 75)
No of cases with raised SAP in Hepatomegaly and CCF	10 (out 0f 51)
No of cases with raised ALP without hepatomegaly	0 (out of 24)
Percentage of raised SAP in CCF	12.5%
Percentage of raised SAP in patients with CCF having hepatomegaly	19.6%



SAP AND HEPATOMEGALY

Table 11

Serum bilirubin

Serum bilirubin	No of cases	Percentage
< 1.2 (Normal)	22	29.3%
1.2 – 3 mg%	43	57.3%
3-5 mg%	7	9.3%
>5 mg%	3	4%

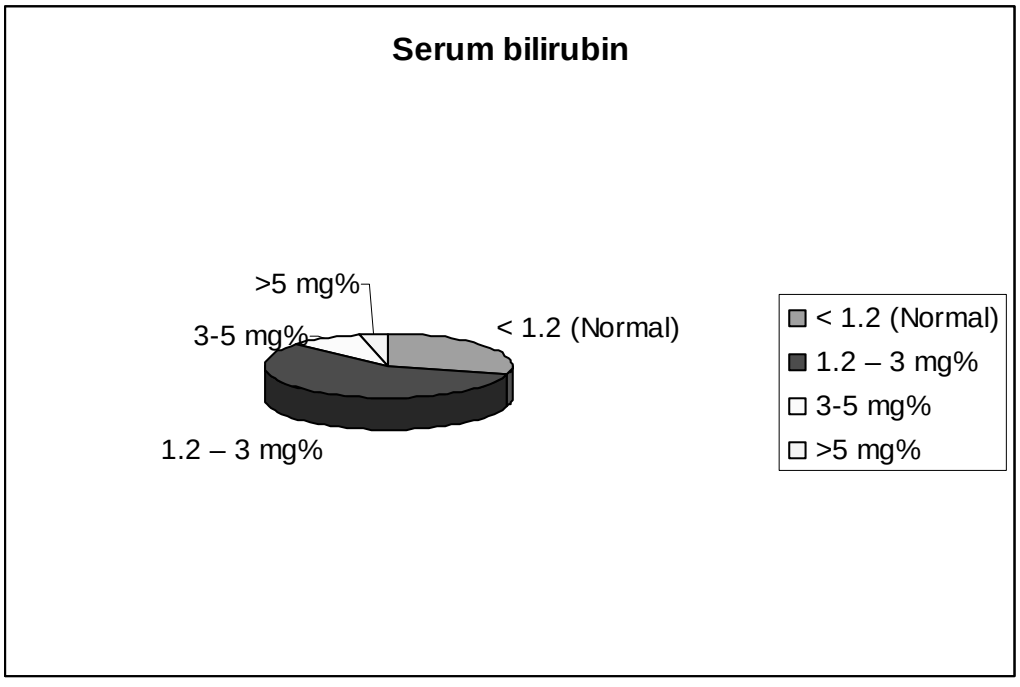


Table 12

Serum bilirubin with remission and exacerbation

No of cases with abnormal LFT	53 (On follow up, 47 showed remission; 6 showed exacerbation)
No of cases showing exacerbation	6
No of cases showing increase of Serum bilirubin on exacerbation	4, 2- no change
Percentage	66.6%
No of cases showing remission	47
No of cases showing reduction of Serum biliruubin on remission	44; 3- showed increase
Percentage	93.6%
Controls	Serum bilirubin were normal in all the controls

p- value is significant – 0.0212.

Table 13

Liver function tests

S No	Test	Normal Range	RESULTS		
			Range	No of patients	percentage
1.	Serum bilirubin	0-3-1.2 mg/dl	< 1.2	22	29.3%
			1.2-3 mg/dl	43	57.3%
			3-5 mg/dl	7	9.3%
			>5 mg/dl	3	4%
2.	AST	Upto 40 I.U	Normal range	36	48%
			Increased	39	52%
3.	ALT	Upto 35 I.U	Normal range	44	58.6%
			Increased	31	41.3%
4.	S.A.P	3 – 13 KA Units	Normal range	65	86.6%
			Increased	10	13.3%
5.	Serum albumin	>3g%	Normal	57	76%
			Reduced	15	20%
			A:G reversal	3	4%
6.	Prothrombin time	Control (12-14 sec), Test abnormal if 1 ½ times greater than control	Normal	33	44%
			Prolonged	42	56%

In controls, no abnormality of LFT was noted.

DISCUSSION

A lot of research has been done in assessing liver function in congestive cardiac failure

In this study, the clinical features and liver function test in congestive cardiac failure due to various etiologies in 75 patients have been compared within and with 20 controls and correlated with various studies in an effort to compare Indian scenario with global picture.

Hepatomegaly

Hepatomegaly was seen in 51 patients out of 75 (68%). The liver enlargement varies from 1cm to 10cm below the RCM in 26% of cases. White et al (1956)[67] found hepatomegaly in 95% of their cases of congestive cardiac failure and Sinha (1960)[84] found hepatic enlargement in 25.5% of cases. Dunn et al (1973)[51] have also described hepatomegaly in 95% of cases. Richman et al (1961)[73] have described hepatomegaly more than 5cm in as many as 50% of patients. None of the controls did have hepatomegaly.

Icterus

Icterus was present in 16(21%) cases. Alcohol induced jaundice and jaundice due to hepatotoxic drugs were ruled out by relevant history taking. Viral hepatitis was ruled out by serological tests for viral markers. Rheumatic heart disease produced the most number of cases with clinically detectable jaundice.

Icterus was least present in patients with Cor pulmonale and hypertensive heart disease. None of the controls had icterus.

White et al [67] have reported clinically apparent jaundice in 20% of cases. Gravin et al [25] and Kubo et al [80] have also described clinical jaundice in less than 20% of cases.

Hyperbilirubinemia

Hyperbilirubinemia was detected in 53 out of 75 cases. The etiologies most associated with hyperbilirubinemia were coronary artery heart disease (73%) and rheumatic valvular heart disease(72%).In majority of cases serum bilirubin did not exceed 3mg/dl.

Kubo et al [80] have reported that serum bilirubin is increased in 20 to 80% of patients with congestive cardiac failure; it rarely exceeds 5mg/d land is usually less than 3mg/dl. Zieve [85] has reported that unconjugated bilirubin is usually higher than conjugated bilirubin. Sherlock [43]and Richman et al [73]have also reported that levels usually range between 1mg/dl and 5mg/dl with the unconjugated form constituting the major fraction. Sherlock [43] has reported that only rarely have levels exceeded 20 mg/dl in patients with severe right-sided heart failure. Richman et al [73]has observed that with improvement of the right-sided heart failure elevated serum bilirubin levels return back to normal quite rapidly over a period of 3-7 days.

S. NO	Authors	% of cases with hyper bilirubinemia
1	Felder et al	52%
2	Sherlock	68%
3	Evans et al	26%
4	White et al	40%
5	Wahi et al	45%
6	Naresh bhu	58%
7	Richman et al	31%
8	This study	70.6%

Marked increase in serum bilirubin was observed in rheumatic valvular heart disease in this study. This correlates with Sherlock's [43] observation that the deep icterus has a correlation with valvular diseases of heart. The severity of failure and duration of failure correlate well with the elevation in serum bilirubin level. The elevated bilirubin level was less than 3mg/dl in 43 cases and more than 5mg/dlin 3 cases who had severe congestive cardiac failure. With remission of congestive cardiac failure, the serum bilirubin returned to normal in 47 cases which correlates with Richman et al [73].

In this study 71% of patients showed an abnormal increase in serum bilirubin levels of which 81% showed mild rise of bilirubin between 1-5mg/dl ; which correlates with Kubo's [80] observation.

Serum aminotransferases

Richman et al [73], Dunn et al [51] and Sherlock et al [43] have reported that elevation in serum aminotransferase levels are seen in 3-50% of patients with right sided heart failure. The wide range in incidence reflects the fact that elevations are seen more commonly in acute congestive heart failure (15-48%) than in chronic failure (3-5%).

Richman has reported that asparate transaminase levels are typically more marked than alanine transaminase levels, the former values ranging from 40-801I.U.This degree of marked elevation is seen in acute heart failure secondary to cor pulmonale or rheumatic heart disease with tricuspid insufficiency, or due to heart failure complicated by shock and hypertension.

In the present study one patient who had severe congestive cardiac failure with shock, showed elevation of asparate transaminase upto 925 I.U. which correlate with Richman's [73] observation.

In the present study 39 cases (52%) of cases showed elevated asparate transaminase levels and 31 cases (41%) of alanine transaminase levels.

With remission 72% of raised asparate transaminase levels and 74% raised alanine transaminase levels returned to normal.

Serum alkaline phosphatase

Richman et al [73] and Sherlock [43] have reported elevation of serum alkaline phosphatase levels in 10-20% of patients with right sided heart failure. Dunn et al [51] however reports that in most patients the levels are within normal limits,rarely do they exceed twice normal. Felders et al [86] have also reported increased serum alkaline phosphatase in 10-20% of patients with congestive cardiac failure.

Elevation of serum alkaline phosphatase levels do not correlate with increases in serum bilirubin or aminotransferases. The highest elevations are usually seen in patients with marked liver enlargement [73].With improvement in the cardiac status serum alkaline phosohatase returns to normal in 1 week.

In the present study 10 cases (13%) showed elevation in alkaline phosphatase levels. With remission, in all cases the serum alkaline phosphatase levels returned to normal. In 51% of cases that had hepatomegaly,20% showed elevated serum alkaline phosphatase levels which correlates with Richman et al's [73] study. In controls, the values were normal.

Serum Proteins:

The serum albumin was decreased in 30-50% of patients with congestive cardiac failure as per Richman et al [73].

The degree of hypoalbuminemia was usually mild and the majority of patients exhibit levels between 2.5and 2.9 g/dl. Dunn et al [51] reported that serum albumin concentrations below 1.5 g/dl are rarely observed and are often associated with marked ascites and edema. With resolution of the underlying cardiac disease, improvement in serum albumin usually occurs over a period of a few months.

According to Richman et al [73],hyperglobuminemia occurs in 37-50% of patients with right sided heart failure and is more common in patients with acute than with chronic heart failure. The elevation tends to be mild, with levels between 3.5 and 4.1 g/dl in the majority of patients. In contrast to other liver tests, the hyperglobulinemia usually does not return to normal after successful treatment of the congestive cardiac failure. The increase in globulin levels and the decrease in albumin levels lead to reversal of Alubumin/Globulin ratio.

In the present study15 cases showed decreased albumin (considering a cutoff 3mg%) ; 3 cases showed increased globulin. Albumin globulin reversal was noted in 3 cases. On remission one patient turned normal. Presence of albumin globulin and hypoalbuminemia were associated with a poor prognosis.

Prothrombin time:

Prothrombin time is prolonged in 80-90% of patients with acute and chronic heart failure according to White et al [67].Richman et al [73] and Dunn et al [51] report that the prothrombin time returns to normal usually 2 to 3 weeks following the successful treatment of heart failure. In the present study 42 of 75 (56%) cases studied showed a prolonged prothrombin time. The prolongation in the prothrombin time ranged from 1$_{1/2}$ times to 2 times that of the control. Controls did not show any variation. Repeated prothrombin time at day 7 did not show any improvement on remission. As the prothrombin time could not be repeated at 3 weeks from remission changes might not have occurred; as suggested by other studies.

SUMMARY

In this study done at Govt. Royapettah Hospital; 75 patients with congestive cardiac failure of varied etiologies were studied. The grades of severity also varied. The liver function tests of these patients were evaluated by measuring the serum bilirubin, Serum transaminases, Serum alkaline phosphatase, serum proteins and prothrombin time. The above functions were evaluated at admission and at the seventh day of admission. The clinical progression was also noted as remission or exacerbation. 20 controls were chosen from healthy individuals of the hospital; 12 were male and 8 female.

Of these 75 patients studied, 44 were male and 31 were female. Of these 1 was between age of 20, 1 between 21 and 30, 8 were between 31 and 40, 19 were between the ages of 41 and 50, 22 were between the ages of 51 and 60, 15 were between the ages of 61 and 70, 8 were between the ages of 71 and 80 and 1 was >80. Among controls, 2 were between the age 21 -30, 5 were between the age 31 – 40; 7 were between the age 41-50 and 6 were above 51.

The duration of cardiac failure was more than 5 years in 38 patients, between 1-5 years in 33 patients and less than 1 year in 4.The etiology of congestive cardiac failure was rheumatic valvular heart disease in 18 patients, cor pulmonale in 13 patients, coronary artery heart disease in 30 patients, hypertensive heart disease in 7 patients and cardiomyopathy in 7 patients.

Clinically apparent jaundice was seen in 16 patients, Hepatomegaly was seen in 52 patients, Ascites was present in 6 patients. Of the 53 patients whose liver functions were deranged,47 attained remission of heart failure and 6 cases showed exacerbation of heart failure.

Analysis of the liver tests showed hyperbilirubinemia in 53 patients, Of these 10 patients had bilirubin more than 3mg. Asparate transaminase was increased in 39 cases and alanine transaminase was increased in 31 cases. Alkaline phosphatase was increased in 10 cases and serum proteins were abnormal in 15 cases with reversal of A/G ratio in 3 cases. The prothrombin time showed prolongation more than 1 ½ times normal in 42 patients.

Analysis according to the various Etiologies shows that patients with coronary artery heart disease (73%) and rheumatic heart disease (72%) showed the most percentage of abnormal liver function tests and patients with hypertensive heart disease (57%) showed least percentage of abnormal heart failure.

Of the 18 patients with rheumatic heart disease,13 patients showed abnormal liver function (72%), Of the 13 patients with cor pulmonale 9 showed abnormal liver function (69%). In 7 patients with hypertensive heart disease 4 showed abnormal liver function (57%), whereas in 30 patients with coronary artery heart disease,22 showed abnormal liver function (73%) 5 out of 7 patients with cardiomyopathy showed abnormal liver function.

Severity of cardiac failure

Serum bilirubin more than 3mg/dl was present with severe congestive cardiac failure. Gross elevation of transaminases was present in severe congestive cardiac failure with hypotension and shock. Hypoalbuminemia and albumin-globulin ratio reversal were found in chronic congestive cardiac failure and were associated with poor prognosis.

Remission

Of the 53 patients with abnormal liver function tests, 47 achieved remission from congestive cardiac failure within 7 days. With remission the hyperbilirubinemia, and the increased asparate transaminase levels and alanine transaminases levels returned to normal. The prothrombin time and serum proteins did not show any marked change

Exacerbation

Exacerbation of congestive cardiac failure was seen in 6 cases. With exacerbation, elevation of serum bilirubin, asparate transaminase, alanine transaminase, alkaline phosphatase and prothrombin time was noted. There was no change in serum proteins.

CONCLUSION

1. The commonest aetiology of cases presenting with features of congestive cardiac failure at Government Royapettah Hospital is coronary artery heart disease.

2. Liver function abnormalities were mostly present in patients with coronary artery disease (73%) and rheumatic valvular heart disease (72%) developing heart failure.

3. Liver function abnormalities were least in patient with hypertensive heart disease (57%) developing heart failure.

4. The serum bilirubin, serum alkaline phosphatase and serum transaminases returned to normal with remission. Serum protein values and the prothrombin time did not change with remission.

5. The serum bilirubin, serum enzymes and prothrombin time were elevated with exacerbation. Serum proteins did not show any change with exacerbation.

6. Severe congestive cardiac failure with hypotension leads to a gross elevation of serum asparate transaminase and alanine transaminase.

7. Serum alkaline phosphatase elevation correlated with the presence of hepatomegaly.

8. Serum bilirubin levels at presentation of more than 5mg, presence of hypoalbuminemia and albumin-globulin ratio reversal were associated with a poor prognosis.

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PROFORMA

Name :

Age / sex :

M R D No :

Presenting Complaints :
- Chest Pain : Duration :
- Breathlessness :
- PND / Orthoonnoea :
- Cough / Expectoration :
- Haemoptysis :
- Pedal Oedema :
- Oliguria :
- Fever :
- Syncope :
- Other Symptoms :

Past H/o
- Diabetes – Duration
- Hypertension
- IHD
- Bronchial Asthma
- Jaundice
- Rheumatic Fever
- Tuberculosis
- Similar Episodes
- TIA
- Exposure to STD

Personal H/o : Smoker
Alcoholic

Family H/o : Hypertension
Diabetes
IHD

General Examination

Consciousness
Orientation
Temperature
Anemia
Jaundice
Cyanosis
Clubbing
Pedal edema
Lymphadenopathy
JVP
Peripheral signs of
Infective endocarditis
Peripheral signs of
Cirrhosis liver

Vital Parameters

Pulse rate
Blood pressure
Respiratory rate

CARDIOVASCULAR SYSTEM

Heart Sounds
Murmurs
Added Sounds
Parasternal Heave
Abnormal Pulsations

RESPIRATORY SYSTEM

Rate
Accessory muscle
Air entry
Rales/ Rhonchi

ABDOMEN

Appearance
Ascites

Hepatomegaly-
Liver span
Tenderness
Consistency

Spleenomegaly

CENTRAL NERVOUS SYSTEM

Higher Functions
Cranial Nerves
Motor System
Sensory System
Cerebellum
Spine&Cranium
Others

DIAGNOSIS

Onset of illness

Acute
Chronic
Acute on chronic

Duration of illness

< 1 Year
1-5 Years
> 5 Years

Investigations

1. Urine routine
2. Hb
3. Tc,Dc,ESR
4. Urea
5. Creatintine
6. Electrolytes
7. Sugar
8. V D R L
9. HbsAG / ANTI HCV
10. ECG
11. X-Ray Chest
12. Echocardiogram

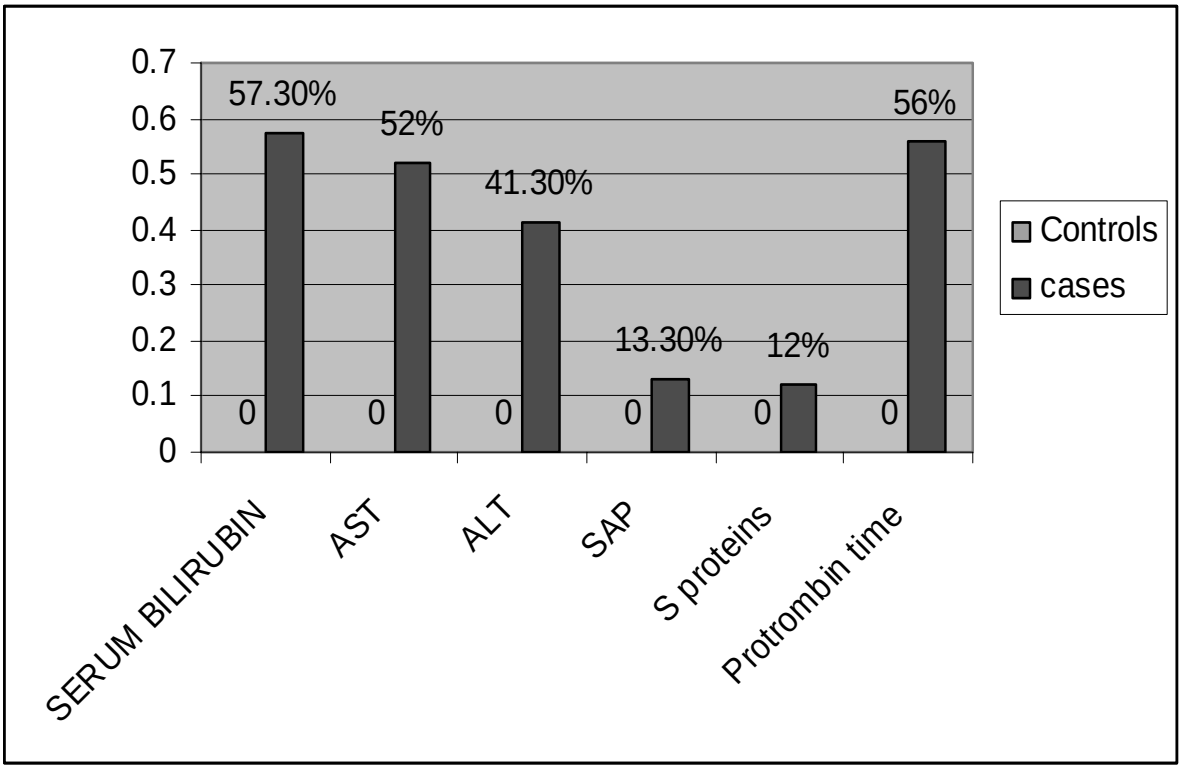
13.LIVER FUNCTION TESTS:

SGOT
SGPT
Alkaline Phosphatase
GGT
S.Bilirubin- Total
Direct
Indirect
Total Proteins
Albumin
Globulin
AG ratio
Prothrombin time

14.USG abdomen

15.Biopsy in selected patients

Abnormalities of liver function tests



MASTER CHART FOR CASES

SI NO	NAME	AGE	SEX	ETIOLOGY	DURATION (Years)			J	H	A	R/E	S.Bil		AST		ALT		SAP		S. PROTEINS						P.T			
																				D1			D7			D1		D7	
1					1	< 5	> 5					D1	D7	D1	D7	D1	D7	D1	D7	T	A	G	T	A	G	C	T	C	T
1.	SAIVARAJ	54	M	CP		*		–	+	–	R	1·8	0·9	36	34	28	30	9	8	6·2	3·2	3	6·4	3·4	3	14	22	14	22
2.	KAMU	44	M	CAHD		*		–	+	–	R	1·6	1·0	60	38	26	24	9	9	5·8	3·0	2·8	6·0	3·1	2·9	12	20	12	19
3.	VASANTHAN	46	M	CAHD		*		–	+	–	R	2·0	1·0	36	30	25	35	9	8	6·2	3·2	3	6·1	3·2	2·9	14	23	14	22
4.	PACHAMUTHU	52	M	CP		*		–	–	–	–	0·8	0·8	35	36	30	32	8	8	6·6	3·4	3·2	6·4	3·4	3	12	18	12	20
5.	PADMANABAN	63	M	CAHD		*		–	–	–	–	1	0·9	40	35	30	32	9	8	6·8	3·4	3·4	6·6	3·4	3·2	12	12	14	16
6.	KANNAPAN	76	M	CAHD			*		+	–	E	1·8	2·6	46	60	42	58	16	22	5·8	3	2·8	5·6	3	2·6	14	21	12	20
7.	AMBIKAPATHY	65	M	CAHD			*	–	–	–	–	0·9	0·8	35	30	32	28	9	8	6·2	3·2	3	6·4	3·3	3·1	14	12	14	14
8.	PATTABIRAM	38	M	CM		*		+	–	–	R	1·8	0·9	40	35	30	32	10	9	5·4	2·4	3	5·4	2·4	3	14	24	14	22
9.	MUNIANDI	94	M	CAHD			*		+	–	–	1	0·9	28	24	25	30	9·5	9	6·2	3·2	3	6·4	3·4	3·2	14	14	12	12
10.	SARGUNADEVI	62	F	CAHD			*		+	–	R	2·2	0·9	28	30	26	24	8·5	8	5	3	3	6·4	3·4	3	14	24	12	22
11.	LAKSHMI	58	F	CAHD		*			+		R	1·7	0·8	30	32	40	32	15	9	5·8	3	2·8	6	3	3	14	12	14	12
12.	DHANASEKAR	48	M	CAHD		*		–	–	–	–	0·8	0·9	30	36	34	30	12	11	5·8	3·2	2·6	6	3	3	14	12	14	14
13.	CHINNASAMY	60	M	CP		*		–	+	+	R	2·0	0·8	34	32	40	31	9	8	5·2	2	3·2	5·4	2	3·4	14	14	14	12
14.	KALIAMOORTHY	75	M	RHD			*	+	+	–	E	1·8	2·6	48	76	42	66	9	9	6	3·9	2·9	6	3·8	2·2	12	23	12	26
15.	ARUMUGAM	60	M	HHD	*			–	+	–	–	0·9	1	26	30	36	32	8·5	8	6	3·2	2·8	6·2	3·2	3	14	14	14	14
16.	KRISHNAVENI	41	F	RHD			*	+	+	–	R	2·4	0·8	56	38	44	38	18	8	5·2	2·8	2·4	5·2	2·8	2·4	12	21	14	24
17.	BALASUBRAMANIAN	44	M	CAHD		*			+	–	R	0·8	1·0	30	32	35	31	9·5	8·6	5·8	3	2·8	6	3·2	2·8	14	12	14	12
18.	CHELLAKANNU	52	M	CAHD		*			+	–	R	1·6	1	28	30	40	32	9	11	5·2	2·8	2·4	5·8	3	2·8	14	12	12	14
19.	SAMINATHAN	59	M	CP			*	–	+	–	R	2·6	0·8	66	40	52	44	10	9	5·7	3	2·4	6	3	3	14	22	12	23
20.	JAYANTHAN	52	M	CAHD		*		–	–	–	–	1.	0·8	26	32	31	32	8	11	6·2	3·2	3	6·2	3·2	3	14	14	14	12

SI NO	NAME	AGE	SEX	ETIOLOGY	DURATION (Years)			J	H	A	R/E	S.Bil		AST		ALT		SAP		S. PROTEINS						P.T			
																				D1			D7			D1		D7	
					1	< 5	> 5					D1	D7	D1	D7	D1	D7	D1	D7	T	A	G	T	A	G	C	T	C	T
21	SEETHALASHMI	40	F	RHD			*	+	+	+	R	18	09	35	32	44	33	17	9	6.2	3	3.2	6.2	3	3.2	14	24	14	24
22	ADIAKALAM	53	M	CAHD		*		-	+	-	R	3.2	1	52	35	62	42	8	8	5.4	3	2.4	5.2	3	2.8	14	24	14	23
23	JEYAPAL	65	M	CP		*		-	_	_	-	1.0	0.9	40	35	32	35	8	10	6.2	3.2	3	6	3	3	14	14	14	12
24	GOVINDARAJ	66	M	CP			*	_	+	_	R	1.6	0.8	55	32	44	35	9	8	5.0	3.2	2.8	5.8	3	2.8	12	14	12	12
25	SHANAZ BEGUM	75	F	HHD		*		-	+	_	R	2.4	1	28	30	40	40	10	10	6.2	3.2	3	6.2	3.2	3	14	22	14	23
26	SARASWATHY	55	F	RHD			*	+	+	_	R	1.7	0.9	40	35	35	32	11	9	6.2	3.2	3	6.2	3.2	3	14	16	14	12
27	RAMAIYAN	45	M	CAHD		*		_	_	_	R	1.9	0.7	46	30	30	30	10	8	5.2	2.2	3.2	5.8	3	2.8	12	12	14	14
28	KUMARESAN	60	M	CAHD			*	_	+	_	R	2.1	0.9	68	50	54	40	11	8	5.2	2.4	2.8	5.8	2.9	2.8	12	23	12	24
29	PENICILLAIAH	75	M	CAHD			*	_	+	_	R	2.3	1.0	30	32	35	33	20	8	6	3	3	6	3	3	14	22	14	22
30	MUNUSAMY	43	M	CP			*	_	+	_	R	1.8	1.0	38	30	40	35	9	9	6	3	3	6	3	3	14	12	14	12
31	SHANMUGAM	36	M	RHD			*	+	+	-	R	2.6	0.8	51	40	46	40	8	9	5.4	2.8	2.8	5.4	2.8	2.8	14	23	12	24
32	PANDIAN	54	M	CAHD		*		_	_	_	R	1.6	0.8	40	35	32	30	10	9	6.6	3.4	3	6.3	3.3	3	14	14	12	12
33	SAROJAMMA	62	F	CAHD			*	+	+	_	E	1.9	1.9	96	126	48	96	12	12	5.4	2.8	2.6	5.4	2.8	2.6	14	23	12	18
34	SHEIK MOHHAMAD	56	M	HHD	*			_	+	_	R	2.4	1.0	72	52	54	32	9	8	5.4	2.8	2.6	5.4	2.8	2.6	14	22	12	24
35	JOHN PAUL	54	M	CP	*			_	+	_	R	3.4	1.0	82	42	66	35	9	9	5.2	2.8	2.4	5.2	2.7	2.5	12	24	12	24
36	MUSTHRI BEGAM	59	F	RHD			*	_	_	_	-	1	0.8	30	32	23	30	8	8	6	3	3	6	3	3	14	12	14	12
37	DEVI	25	F	HHD			*	_	+	_	R	1.8	1.0	65	40	54	40	10	8	6.2	3.2	3	6.2	3.2	3	14	24	14	23
38	MARIAM	45	F	CP		*		_	+	_	R	1.9	1.0	40	35	35	43	11	10	6	4	2	6	3.8	2.2	14	14	12	12
39	MAHENDRAN	56	M	CM			*	+	_	_	R	2.4	0.9	65	42	58	42	9	8	5.9	3.1	2.8	6	3.1	2.9	14	22	14	22
40	RAMANI	35	F	RHD		*		+	+	_	R	2.6	0.8	50	42	40	36	18	9	6	3	3	6	3	3	14	22	14	24

SI NO	NAME	AGE	SEX	ETIOLOGY	DURATION (Years)			J	H	A	R/E	S.Bil		AST		ALT		SAP		S. PROTEINS									
																				D1			D7			D1	D7		D7
					1	< 5	> 5					D1	D7	D1	D7	D1	D7	D1	D7	T	A	G	T	A	G	C	T	C	T
41	PONNAMAL	62	F	CP	*			–	+	–	–	0.9	1	40	35	35	32	9	9	6.2	3	3.2	6.2	3	3.2	12	12	14	14
42	VALLIAMMAL	65	F	CAHD		*		+	+	–	R	3.8	1.2	925	196	628	104	22	9	6	3.3	2.7	6	3.4	2.6	14	24	14	24
43	ZABIYA BEE	72	F	CAHD		*		–	+	–	R	1.8	1	48	32	40	32	8	10	5.8	3	2.8	6	3	3	12	22	12	24
44	NAGAMMAL	44	F	HHD			*	–	–	–	–	1	0.9	28	30	28	30	11	11	6	3.2	2.8	6	3.2	2.8	14	12	14	12
45	VALLI	43	F	CM		*		–	–	-	–	0.8	1.0	30	32	35	30	10	12	6	3	3	6.2	3.2	3	14	14	14	14
46	GOVINDAMMAL	41	F	RHD			*	–	+	–	R	3.6	1.0	136	58	76	40	9	8	6.6	3.8	2.8	6.6	3.8	2.8	14	24	14	24
47	RAJESWARI	65	F	CM			*	–	+	+	R	2.4	4.6	56	244	48	86	8	8	6.6	3.4	3.2	T	3.6	3.3	14	22	12	24
48	PRADEEP	15	M	RHD		*		–	+	–	–	0.9	0.8	40	36	36	30	8.5	9.5	6	3	3	6.4	3.4	3	12	12	12	12
49	MARIAMMAL	65	F	CAHD			*	–	+	–	R	1.8	0.9	48	40	26	30	9	8.5	6	3.2	3	6.2	3.2	3	14	21	14	21
50	DURAI	36	M	RHD		*		–	–	–	–	1	1	36	33	35	34	9	8	6.2	3.2	3	6.4	3.4	3	14	12	14	12
51	PACCHAIAMMAL	75	F	CAHD			*	+	+	–	R	5	1.0	98	40	45	36	10	11.5	6.2	3.2	3	6.4	3.2	3.2	14	23	14	23
52	MANNAMAL	80	F	RHD			*	–	–	–	R	1.8	0.8	66	35	56	40	12.5	11	5.8	2.8	3	5.8	2.8	3	14	22	14	22
53	ARJUANAN	62	M	CAHD			*	–	+	–	R	3.2	1	62	42	42	30	9.5	9	6	3	3	6.2	3.2	3	12	26	12	26
54	VELAPPAN	60	M	CAHD		*		–	–	–	R	5	1.0	76	50	68	40	9.5	9	5.2	2.7	2.5	5.2	2.8	2.4	14	24	14	26
55	DHANAMMA	50	F	CAHD		*		+	–	–	R	4.3	0.8	180	60	78	35	12.5	8	6.2	3.8	2.4	6.6	4	2.6	12	24	14	24
56	SAMSHAD BEEVI	60	F	CAHD		*		–	+	–	R	2.0	0.9	45	40	35	32	10	9	6.6	4	2.6	T	3.6	3.4	12	24	14	23
57	SAM MOSES	56	M	CP		*		–	+	–	R	1.6	0.7	288	88	96	48	20	9	6.8	3.5	3.3	T	3.8	3.2	12	12	14	14
58	KANNIVELU	70	M	CAHD			*	+	–	+	E	5.2	6.2	156	172	76	88	9.5	10	6.8	3.8	2.2	6.4	3.6	2.4	14	24	12	28
59	SENKENI	41	F	RHD			*	–	–	–	–	1	0.9	32	30	28	30	9	11	6	3	3	6.6	3.6	3	14	14	12	12
60	JUNAITHA BANU	53	F	RHD			*	–	+	–	R	1.8	0.9	54	40	48	32	8	8	6	3	3	6.4	3.4	3	12	24	12	28

SI NO	NAME	AGE	SEX	ETIOLOGY	DURATION (Years)			J	H	A	R/E	S.Bil		AST		ALT		SAP		S. PROTEINS						P.T			
																				D1			D7			D1		D7	
					1	< 5	> 5					D 1	D 7	D 1	D 7	D 1	D 7	D 1	D 7	T	A	G	T	A	G	C	T	C	T
61	ABDUL SUKKUR	42	M	CAHD		*		-	+	-	-	1.0	1.0	40	32	40	35	8.5	9	6.2	3.2	3	6.4	3.4	3	12	16	12	14
62	INDIRANI	35	F	RHD			*	+	+	-	R	2.6	0.9	136	64	58	44	18	9	6	3	3	6.6	3.4	3.2	14	24	14	28
63	IRUDHAYA MARY	40	F	RHD			*	-	-	-	R	1.8	1.0	65	46	52	44	10.5	11	6.2	3.2	3	6.8	3.6	3.2	12	21	12	21
64	ANNAMALAI	50	M	CM			*	-	-	-	E	2.4	3.6	96	152	62	126	11	12	6.4	3.4	3	6.6	3.6	3	12	26	14	31
65	CHOCKAMMAL	44	F	HHD			*	-	+	-	R	1.8	0.9	56	35	30	32	8	8.5	6	3	3	6	3	3	14	14	14	14
66	SENTHAMARAI	67	M	CAHD		*		-	+	-	R	1.1	0.8	48	40	40	35	11	9	5.8	2.9	2.9	5.8	2.9	2.9	12	12	12	12
67	ZAKIA BANU	45	F	RHD			*	+	+	+	R	1.8	2.6	68	96	48	66	9.5	10	6	3	3	6.4	3.4	3	14	24	14	24
68	SINGARAM	71	M	CP			*	+	+	-	R	2.4	1.0	58	40	56	42	10.5	8	6.2	3.2	3	6.2	3.2	3	14	22	14	24
69	GANESAN	68	M	CAHD			*	-	+	-	-	0.9	0.9	40	35	40	35	9.5	9	6	3.2	2.8	6.1	3.3	2.8	14	14	14	14
70	VEDHACHALAM	60	M	CM			*	+	+	+	E	3.2	3.2	146	268	86	106	11	11.5	5	2.6	2.4	5.1	2.7	2.4	12	20	14	26
71	ARPUTHARAJ	62	M	CM		*		-	-	-	-	1.0	0.8	36	28	35	40	12	12	6.2	3.2	3	6.4	3.4	3	12	12	14	26
72	NATARAJAN	58	M	HHD		*		-	-	-	-	1.0	1.0	40	35	26	31	8	10.5	6.4	3.4	3	6.4	3.4	3	14	12	12	12
73	MUMAITHA BEE	40	F	RHD		*		-	+	-	R	1.8	0.9	56	40	48	40	17	8	6.6	3.6	3	6.6	3.4	3.2	12	24	14	26
74	MANOHARI	42	F	RHD			*	-	-	-	-	0.9	0.7	32	30	28	32	9.5	11	6	3.2	2.8	6.4	3.4	3	12	12	12	12
75	SEENIVASAN	56	M	CP	*			-	+	-	-	0.8	1.0	40	35	30	28	10	12	6.4	3.4	3	6.6	3.6	3	14	14	14	14

J -- JAUNDICE
H – HEPATOMEGALY
A—ASCITES
R/E—REMISSION/ EXACERBATION
P.T -- PROTHROMBIN TIME
C P – COR PULMONALE
C M - CARDIOMYOPATHY

S.BIL – SERUM BILIRUBIN
AST – ASPARTATE TRANSAMINASE
ALT – ALANINE TRANSAMINASE
SAP- SERUM ALKALINE PHOSPHATASE
HHD – Hypertensive Heart Diseases
RHD – Rheumatic Heart Disease

MASTER CHART FOR CONTROLS

SI NO	NAME	AGE	SEX	J	H	A	S.Bil		AST		ALT		SAP		S. PROTEINS						P.T			
															D1			D7			D1			D7
							D1	D7	D1	D7	D1	D7	D1	D7	T	A	G	T	A	G	C	T	C	T
1.	MURALI	42	M	–	–	–	0·8	0·8	38	36	34	32	4	6	5·8	3·8	2·0	5·8	3·8	2·0	12	14	12	14
2	GOPI	28	M	–	–	–	0·7	0·7	30	32	30	28	6	8	6·0	4·0	2·0	6·0	4·0	2·0	14	14	14	14
3	LOGANATHAN	45	M	–	–	–	0·6	0·6	28	30	32	30	8	8	6·2	4·1	2·1	6·2	4·1	2·1	12	12	12	14
4	BABU	51	M	–	–	–	0·9	0·8	26	24	22	20	10	12	6·6	4·0	2·6	6·6	4·0	2·6	12	14	12	12
5	KUPPUSAMY	52	M	–	–	–	1·1	1·1	28	30	30	30	10	8	7	4	3	7	4	3	14	14	12	14
6	VASANTHA	48	F	–	–	–	0·6	0·6	26	26	22	20	7	9	5·9	3·6	2·4	6·2	4	2·4	14	12	14	14
7	JEYASEELI	54	F	–	–	–	0·7	0·8	28	28	20	20	6	4	6·2	4·2	2·2	6	4·1	2	12	12	12	12
8	MANIKANDAN	27	M	–	–	–	0·4	0·4	24	24	21	21	7	8	6·3	4·2	2·1	6·3	4·2	2·1	12	12	12	14
9	RAMSESH	33	M	–	–	–	0·8	0·8	28	28	22	22	7	7	6·2	4·2	2	6·1	4·1	2	12	14	12	14
10	SHANTHI	49	F	–	–	–	0·6	0·6	36	36	32	32	6	6	6·0	4	2	6·0	4	2	12	14	12	16
11	KAVITHA	35	F	–	–	–	0·4	0·6	32	32	28	28	4	4	6·1	4	2·1	6·1	3·9	2·2	14	14	12	14
12	LAKSHMI	46	F	–	–	–	0·7	0·8	34	32	24	24	3	5	5·8	4	1·8	5·8	4	1·8	12	14	12	14
13	KARPAGAM	32	F	–	–	–	0·8	0·7	30	26	20	22	9	8	5·8	3·6	2·2	5·8	3·6	2·2	12	12	12	14
14	SEKAR	49	M	–	–	–	0·9	1·0	26	26	24	24	11	10	5·9	4	1·9	5·9	4	1·9	12	14	12	12
15	SAMUEL	56	M	–	–	-	1·0	0·8	32	32	24	24	10	11	6·1	3·8	2·3	6·1	3·8	2·3	14	14	12	14
16	RAMANATHAN	53	M	–	–	–	1·1	1·0	30	26	26	22	6	6	6	4	2	6	4	2	12	12	12	16
17	NOUSHADH	51	F	–	–	–	0·9	1·1	34	30	24	26	7	7	6·6	4	2·6	6·4	4	2·4	12	12	12	14
18	EDWARD	32	M	–	–	–	1·0	0·7	28	20	20	18	8	6	6·0	4	2	6	4	2	12	14	12	16
19	MALLIGA	39	F.	–	–	-	0·7	0·9	26	26	28	22	9	8	6	3·6	2·4	6	3·6	2·4	14	14	12	12
20	CHINNAIAH	47	M	–	–	–	0·6	0·6	22	20	18	19	4	4	6·4	4·0	2·4	6·4	4	2·4	14	14	14	14

IX